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The Journal of Laboratory and Clinical Medicine

VOL. IV. ST. LOUIS, NOVEMBER, 1918 No. 2

ORIGINAL ARTICLES

THE CLINICAL PATHOLOGY OF MUSTARD GAS (DICHLORETHYL-SULPHIDE) POISONING*

BY GEORGE R. HERRMANN, M.S., M.D., ANN ARBOR, MICHIGAN

IN the rapidly accumulating mass of literature on war gassing there are practically no reports on the clinical laboratory aspects of the condition. Even the most ordinary routine examinations as practiced daily in the smallest civilian hospital are unrecorded in the clinical reports on gassing sent from the front. Occasionally in the French reports some fragmentary laboratory observation is included. Mandel and Gibson[1], speaking of the complications of mustard gas poisoning say that albuminuria is not uncommon, but that true nephritis has been rare in their experience. They comment that this is remarkable considering the frequent extensive burns of skin and mucous membranes. Pissarello[2] reports that in his series of sixty cases the urine was always negative to tests for sugar and albumin. If the observations on the urinary changes are few, as shown by the preceding, those on the blood changes are still more rare. Miller[3] has recorded observations on the blood changes found in the more or less chronic stages of gassed cases; and, although not specifically stated, some of these may have been cases of mustard gas poisoning. The exigencies of field and camp, of the field and base hospital, in the active sectors where cases of gassing would be met, have undoubtedly been such as to necessitate a sacrifice of the laboratory aspects of the condition. Further, the lack of complete laboratory facilities for the routine and special examinations, as well as of trained laboratory workers, would discourage attempts in this line of research.

Through the cooperation of Captain Lester Roos, and at the request of Doctor A. S. Warthin an opportunity was afforded me of making observations upon

*From the Pathological Laboratory of the University of Michigan, Ann Arbor, Michigan.

the blood and urinary changes in a series of cases gassed with mustard gas. In thirty cases, we were fortunate in having a very interesting variety from the most severe types, those which resulted fatally, to those showing only the slightest lesions such as the most mild type of conjunctivitis. Nine of the severe cases, on whom the observations were fairly complete, and a tenth group of the mild cases, will be reported at this time. The latter suffered only from conjunctivitis and minor burns of the hands and fingers, and time did not permit any extensive study of this type of case. Unfortunately, our cases were not accessible until the tenth day after the gassing, and then no clinical laboratory was at hand in which our work could be carried out. Further, the more or less inaccessibility of the camp made the organization and maintenance of the laboratory a problem. The lack of adequate assistance during the emergency also rendered it impossible for us to do the laboratory work as completely as we had hoped. Nevertheless, we succeeded in getting a fairly complete record of the disturbances of function in the severe cases. The results determined the management and application of therapeutic measures, and the favorable effects of the instituted treatment were likewise noted. Another encouraging feature of this work is the definite and constant regularity of the results. The step-like gradation in the severity of the cases finds a parallel in the results of the various laboratory examinations; and the changes in the blood and urine show a gradual improvement, uniformly, under the adopted methods of treatment.

THE LABORATORY TESTS AND METHODS EMPLOYED

The laboratory work was carried out according to the routine methods of any well-regulated hospital. Daily complete 24-hour urine specimens were collected in clean, well corked, dark glass, two liter bottles, each patient having his own bottle throughout the period in the hospital. The urine samples were examined daily. The specimen was measured and mixed in a graduated glass cylinder. The physical characteristics of the urine were noted and the reaction to red and blue litmus paper was determined. The specific gravity was taken with a urinometer graduated for work at room temperature. A sample of urine was tested for reducing substances, especially glucose, with Fehling's solution. The specimens were very carefully examined for albumin, routinely, by the Heller's fuming nitric acid ring test, and the acetic acid (8 per cent) and potassium ferrocyanide method. In many instances, and especially, if there was any question as to the reaction, the heat and nitric acid, and the heat and acetic acid (3 per cent) tests, were used. The dilute ferric chloride test for the heat labile, Burgundy-red reaction of diacetic acid, as the index of acidosis, was carried out for some time in each case.

An estimate of the renal function or efficiency was obtained by the quantitative percentage determination of urea and sodium chloride, and the calculation of the daily 24-hour output of these substances, in the daily 24-hour urinary excretion.

The quantitative urine urea was determined in each case by the method of Marshall and Van Slyke in which urease, the urea splitting enzyme, obtained from the soy bean, is used to hydrolyze the urea and yield ammonia.[4, 5, 6, 7] The quantitative urine chloride estimations were made by the modified Volhard's method, in which the albumin-free urine is titrated against a solution of silver nitrate, containing 29.06 grams per liter, 1 c.c. of this solution, corresponding to 0.01 grams of sodium chloride. The ammonium thiocyanate solution used to estimate the excess of the $AgNO_3$ solution used by titration was of such a strength that 2 c.c. neutralized 1 c.c. of the silver nitrate solution. The nitric acid and iron salt indicator was used.[4, 5, 6, 7]

A few of the special examinations and tests were made on the urines. The diazo reaction of Ehrlich with sulphanilic hydrochloric acid and sodium nitrite was tried regularly for a part of the course of each case. Likewise a test for urobilinogen with paradimethylamino-benzaldehyde was carried out fairly routinely, as long as the reagent was at hand. The bromine water oxidizing method was used in the examination of the urine for melanin. Gmelin's nitric acid test and the foam test for bile pigments were employed

in each case. Besides this complete chemical examination the centrifugated sediment of the urine was regularly and carefully examined microscopically.

The functional efficiency of the kidneys was further determined by estimating the percentage of phenolsulphonephthalein that was excreted, when the Rowntree and Geraghty renal functional test was applied. The quantitative estimations were made with a Dunning colorimeter. Unfortunately, the phenolsulphonephthalein and the colorimeter apparatus could not be obtained until late, that is, when the patients were convalescing.

Another index of the secretory ability of the kidney was determined by the estimation of the quantity of urea in the blood. Van Slyke's modification of Marshall's urease method was employed in this procedure as it had been in the case of the urine urea determinations. The usual enumeration of red and white blood cells, differential counting of the leucocytes and estimation of the hemoglobin were carried out. The red and white blood cells were counted in a Thoma-Zeiss hemacytometer. The hemoglobin was estimated by a Gower-Sahli hemoglobinometer and a Tallquist scale. Cover-glass blood smears were made and the preparations were stained with Wright's blood stain for differential counting. The sputum and stools were examined when indicated.

Culture media were not at hand for a complete bacteriologic examination in these cases. In the marked stage of secondary furunculosis, many smears from very young furuncles and also smears of the pus in the more mature lesions were made and stained with various staining solutions.

THE CASES

The material has been arranged and is presented according to the severity of the cases. Beginning with Case I, the most severe, each succeeding case, in order, is less severe down through the nine cases. The seven severe cases were all gassed on the same day, June 27, but were seen for the first time by an army medical man on July 4. In Case Group No. X all four members of which are very mild, this same order is maintained; Case X-A being the most severe of that group, and the last case practically an untouched individual, who had been with the other men, but who was apparently unsusceptible to the concentrations to which the other men had reacted. The remainder of the thirty cases were similarly very mild and the laboratory examinations revealed no departures from the normal.

The blood pressure readings were not made, because the severe skin burns and especially the deep ulcerations in the bends of the elbows, made the procedure too painful in the more serious cases and it was not considered worth while in the mild ones.

The temperature, pulse and respiration tables for each case are followed by the laboratory data of the changes in the urine, blood urea and blood, with other special examinations according to the indications.

CASE I.—Patient had been severely gassed ten days before and was moribund when the blood specimen was taken. Death occurred nine hours later. Almost the entire skin surface was involved; secondary infection was marked, and a foul-smelling gangrenous layer, saturated with pus, covered the body.

TEMPERATURE, PULSE, AND RESPIRATION

		T.	P.	R.
June 27	7:30 P.M.	97.6	90 (?)	20 (?)
June 28		98.5	99 (?)	20 (?)
June 29		98.8	99 (?)	20 (?)
June 30		99.8	104 (?)	20 (?)
July 1	A.M.	100.	105 (?)	20 (?)
July 2	A.M.	98.2	87 (?)	20 (?)
	P.M.	102.	152	28
July 3	6:00 A.M.		124	
	12:00 M.	100.6	110	28 (?)
	6:00 P.M.	102.8	128	28 (?)

TEMPERATURE, PULSE, AND RESPIRATION (*Cont'd*)

				T.	P.	R.
July	4		A.M.	101.6	158	28 (?)
			P.M.	103.2	150	28 (?)
July	5		A.M	104	140	26
		4:00	P.M.	103.6	152	26
		9:00	P.M.	104	162	28
July	6	8:00	A.M.	103	140	28
		12:00	M.	103	142	28
		4:00	P.M.	102.4	136	24
		7:45	P.M.	100	136	28
		10:15	P.M.	101	136	32
July	7	2:00	A.M.	100.2	140	28

URINE AND BLOOD UREA

	PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE	SUGAR GLUCOSE	ALBUMIN	ACIDOSIS DIACETIC ACID	RENAL FUNCTIONAL EFFICIENCY				DIAZO SUB.			PIGMENTS		
DATE	URINE OUTPUT AMT. IN 24 HRS. / REACTION / SPECIFIC GRAVITY	FEHLING'S SOL.	HELLER'S HNO_3 RING TEST	ACETIC AC. FERROCYANIDE	FERRIC CHLORIDE	QUANT. UREA GM. PER 100 C.C.	QUANT. CHLORIDE GM. PER 100 C.C.	UREA OUTPUT IN 24 HRS.	CHLORIDE OUTPUT IN 24 HRS.	SULPHANILIC AC. EHRLICH'S DIAZO	DIMETHYLAMINOBENZALDEHYDE	UROBILINOGEN	BROMIN WATER MELANIN	GMELIN'S TEST FOR BILE	FOAM TEST FOR BILE
July 7	60 c.c. P.M.* Acid 1020 (Anuria**)	Neg.	Pos.	Pos.	Neg.	0.13	0.18	—	—	—	—	—	—	—	—
7	BLOOD UREA P.M. .1104 gm. Urea per 100 c.c.														
7	COLOR OF URINE Dirty yellow. Turbid.	URINARY SEDIMENT Great showers of granular casts. Many fragmented casts. Much debris. Masses of epithelial cells (bladder and few renal). Leucocytes. Clusters of red blood cells. Amorphous urates.													

*P.M. Bladder urine postmortem.
**Patient practically had had anuria during the last twenty-four hours of life.

BLOOD

Erythrocyte count,		3,650,000
Hemoglobin,		70%
White cell count,		13,200
Differential White Count:		
Polynuclears		
Neutrophile	88%	
Eosinophile	4%	
Lymphocytes		
Large	1%	
Small	2%	
Transitionals	2%	
Myelocytes, Neutrophile	3%	

The blood platelets were not increased. The red cells show no changes. No nucleated red cells were found.

CASE II.—This was likewise a case of very severe gassing. The first blood count was made eleven days after being gassed. At that time there was a diffuse suppurative gangrenous process resulting from an extreme secondary infection of the necrosing skin. Active measures were taken to lessen the degree of the pyogenic process. The last blood count was done on the day of his death, four weeks after gassing.

TEMPERATURE, PULSE, AND RESPIRATION

		T.	P.	R.	
June 30		98.	72	20	
July 1		100.4	105	24	
July 2	A.M.	98.6	80	20	
	P.M.	98.8	100	18	
July 3	A.M.	100.6	112	24	
	P.M.	100.8	110	20	
July 4	A.M.	102.6	100	20	(?)
July 5	5:00 A.M.	102.6	158	32	
	4:00 P.M.	103.6	160	32	(?)
	9:00 P.M.	103.	152	34	
July 6	4:00 A.M	103.	148	32	
	12:00 M.	103.	150	32	(?)
	4:00 P.M.	101.	152	28	
	5:45 P.M.	103.6	152	28	
July 7	4:30 A.M.	102.2	148	36	
	7:00 A.M.	102.	148	38	
	1:00 P.M.	102.2	140	36	(?)
	4:30 P.M.	101.6	150	36	
	8:30 P.M.	102.4	152	38	
	10:30 P.M.	100.	150	34	
July 8	4:00 A.M.	102.6	152	36	
	8:00 A.M.	103.	136	36	
	1:00 P.M.	102.2	138	38	
	4:00 P.M.	100.	136	36	
	8:00 P.M.	103.4	140	38	
July 9	4:00 A.M.	101.6	148	38	
	7:30 A.M.	100.8	148	38	
	12:00 M.	100.2	116	28	
	4:00 P.M.	100.8	104	30	
	8:00 P.M.	100.4	120	32	
	12:00 P.M.	100.5	122	32	(?)
July 10	4:00 A.M.	100.6	118	30	
	8:00 A.M.	100.6	128	32	
	12:00 M.	100.4	120	30	
	4:00 P.M.	101.	130	30	
	7:45 P.M.	102.4	128	27	
	12:00 P.M.	101.2	122	28	
July 11	4:00 A.M.	100.8	126	25	
	12:00 M.	101.	136	36	
	4:00 P.M.	103.	130	32	
	7:00 P.M.	101.			
	8:30 P.M	99.	120	26	
July 12	12:30 A.M.	99.4	133	28	
	4:00 A.M.	99.2	120	26	
	8:00 A.M.	100.8	106	30	
	10:00 A.M.	101.2			
	12:00 M.	108.8	126	26	
	3:00 P.M.	100.4			
	4:00 P.M.	102.3	139	34	
	5:30 P.M.	100.4			
July 13	1:30 A.M.	101.	120		
	5:00 A.M.	102.4	124		
	7:00 A.M.	100.	118	22	
	8:00 A.M.	101.2	120	24	
	12:00 M.	102.2	126	30	
	2:30 P.M.	102.2	128	30	
	4:00 P.M.				
	5:00 P.M.	103.	132	30	
	8:00 P.M.	102.	130	30	
	10:00 P.M.	102.	134	30	
	11:15 P.M.	102.	130		
July 14	2:00 A.M.	100.6	124	28	
	3:00 A.M.				
	4:00 A.M.	100.2	126	24	
	6:00 A.M.				

TEMPERATURE, PULSE, AND RESPIRATION (*Cont'd*)

		T.	P.	R.
July 14	8:00 A.M.			
	12:00 M.	101.	124	
	4:00 P.M.	102.5	140	34
	8:00 P.M.	102.	130	
	10:00 P.M.	103.	132	
	10:45 P.M.	103.5	130	
July 15	3:30 A.M.	101.	126	24
	6:00 A.M.			
	7:00 A.M.	100.5	118	24
	12:00 M.	103.6	134	30
	4:00 P.M.	102.5	140	34
	8:30 P.M.	102.2	125	
	9:00 P.M.	103.2	126	
	12:00 P.M.	102.2	97	
July 16	1:00 A.M.	101.2	100	
	4:00 A.M.	101.6	115	
	5:00 A.M.	101.8	119	
	7:00 A.M.	100.	121	
	8:00 A.M.	106.6	128	34
	12:00 M.	101.	116	32
	4:00 P.M.	102.2	110	
	8:00 P.M.	103.	120	
	10:00 P.M.	99.8	124	
	10:30 P.M.	99.8	125	
	11:00 P.M.		110	
	11:30 P.M.		120	
	12:00 P.M.	102.	115	
July 17	12:30 A.M.			
	2:30 A.M.	102.6	116	
	4:00 A.M.	101.2	115	
	4:30 A.M.			
	5:00 A.M.	101.2	126	
	6:00 A.M.	99.2	126	
	8:00 A.M.	100.6	120	30
	12:00 M.	100.4	112	28
	4:00 P.M.	100.4	128	28
	8:00 P.M.	101.8	125	
	10:00 P.M.	99.8	120	
	12:00 P.M.	101.	120	
July 18	2:00 A.M.	98.8	115	
	4:00 A.M.	98.8	120	
	8:00 A.M.	100.	126	32
	1:00 P.M.	100.4	116	28
	5:00 P.M.	100.6	128	
	8:00 P.M.	101.8	120	
	12:00 P.M.	102.	130	
July 19	4:00 A.M.	100.2	124	28
	8:00 A.M.	100.	128	28
	1:00 P.M.	100.6	120	28
	4:00 P.M.	101.4	120	28
	8:00 P.M.	101.6	120	
	12:00 P.M.	101.6	120	28
July 20	4:00 A.M.	101.4	125	
	4:30 A.M.	100.2		
	8:00 A.M.	99.8	120	30
	12:00 M.	100.2	124	32
	4:00 P.M.	101.4	124	34
	8:00 P.M.	102.2	120	
	10:00 P.M.	101.2	124	
	12:00 P.M.	101.2	125	
July 21	4:00 A.M.	101.4	120	
	6:00 A.M.	99.8	105	

TEMPERATURE, PULSE, AND RESPIRATION (*Cont'd*)

		T.	P.	R.
July 21	8:00 A.M.	99.8	124	30
	12:00 M.	101.2	124	30
	4:00 P.M.	101.6	128	32
	8:00 P.M.	102.4	130	
	10:00 P.M.	100.	120	
	12:00 P.M.	101.6	122	
July 22	2:00 A.M.	100.2	124	
	4:00 A.M.	101.2	126	
	6:00 A.M.	98.6	120	
	8:00 A.M.	99.6	130	36
	11:00 A.M.		136	50
	12:00 M.	101.6	140	50
	4:00 P.M.	102.	152	52
	5:00 P.M.		160	58

URINE AND BLOOD UREA

	PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE			SUGAR GLUCOSE	ALBUMIN	ACIDOSIS DIACETIC ACID		RENAL FUNCTIONAL EFFICIENCY			DIAZO SUB.		PIGMENTS		
DATE	URINE OUTPUT AMT. IN 24 HRS.	REACTION	SPECIFIC GRAVITY	FEHLING'S SOL.	HELLER'S HNO_3 RING TEST	ACETIC AC. FERROCYANIDE	FERRIC CHLORIDE	QUANT. UREA GM. PER 100 C.C.	QUANT. CHLORIDE GM. PER 100 C.C.	UREA OUTPUT IN 24 HRS.	CHLORIDE OUTPUT IN 24 HRS.	SULPHANILIC AC. EHRLICH'S DIAZO	DIMETHYLAMINOBENZALDEHYDE UROBILINOGEN	BROMIN WATER MELANIN	GMELIN'S TEST FOR BILE	FOAM TEST FOR BILE
July	c.c.										G.					
8	1850	Acid	1018	Neg.	Pos.?	Pos.?	Neg.	—	0.16	—	2.96	—	—	—	Neg.	Neg.
9	1470	"	1024	Neg.	Pos.	Pos.	Neg.	—	0.24	—	3.53	—	—	—	Neg.	Neg.
10	1000	"	1020	Neg.	Pos.	Pos.	Neg.	0.53	0.10	5.30	1.00	—	—	—	Neg.	Neg.
11	1650	"	1012	Neg.	Pos.	Pos.	Neg.	—	0.22	—	3.33	Neg.	—	Neg.	Neg.	Neg.
12	1150	"	1013	Neg.	Pos.	Pos.	Neg.	0.74	0.40	8.51	4.60	Neg.	—	Neg.	Neg.	Neg.
13	1200	"	1015	Neg.	Pos.?	Pos.	Neg.	0.38	—	4.56	—	Neg.	—	Neg.	Neg.	Neg.
14	2000	"	1011	Neg.	Pos.	Pos.	Neg.	1.80	—	36.0	—	Neg.	—	Neg.	Neg.	Neg.
15	— *	"	1015	Neg.	Pos.	Pos.	Neg.	1.35	—	—	—	Neg.	—	Neg.	Neg.	Neg.
16	1550	"	1013	Neg.	Pos.	Pos.	Neg.	0.54	0.30	8.37	4.65	Neg.	Pos.	Neg.	Neg.	Neg.
17	500*	"	1024	Neg.	Trace	Trace	Neg.	—	0.50	—	2.50	—	Pos.	—	Neg.	Neg.
18	730*	"	1020	Neg.	"	"	Neg.	0.84	0.52	6.16	3.79	—	Pos.	—	Neg.	Neg.
19	750*	"	1015	Neg.	"	"	Neg.	0.54	0.66	4.05	4.95	—	Neg.	—	Neg.	Neg.
20	800*	"	1013	Neg.	Neg.	Neg.	Neg.	—	0.44	—	3.52	—	—	—	—	—
21	1075*	"	1007	Neg.	Trace	Trace	Neg.	0.35	0.54	3.76	5.80	—	—	—	—	—
22	1475*	"	1008	Neg.	"	"	Neg.	—	0.42	—	6.19	—	—	—	—	—

	BLOOD UREA	URINARY SEDIMENT
10	.036 Gm. per 100 c.c.	
	COLOR OF URINE	
8	Deep red brown.	Amorphous urates. Few granular casts. Bladder and kidney epithelial cells. Many leucocytes. Few red blood cells.
11	Brownish yellow.	Amorphous urates. Granular casts. Leucocytes. Epithelial cells, plus the sediment of some alkaline fermentation—triple phosphates especially.
13	Dark brown.	Excess of uric acid crystals. Amorphous urates. Large number of red blood cells. Few granular casts and epithelial cells.
15	"	Incontinence, no specimen collected.
16	Amber	Much improved. Amorphous urates. Leucocytes. Few fragmented granular casts. Epithelial cells. Few bacteria (contamination). No red blood cells.
17	Dark amber.	Few amorphous urates. Few leucocytes. Few granular and epithelial cells. Bacteria.
18	"	Excessive amount of uric acid and amorphous urates coloring the sediment bright red. Few leucocytes. Few granular casts. Few renal epithelial cells.
19	Light amber.	Sediment is much improved. Few amorphous urates. Few granular epithelial cells. Few leucocytes. One or two hyaline casts.
20	Amber.	Apparently much improved. Few amorphous urates. Leucocytes, and granular epithelial cells.
21	"	Abundant urates. Few hyaline and fragmented granular casts. Few granular epithelial cells. Few leucocytes.
22	"	Large amount of amorphous urates. Many uric acid crystals. Numerous hyaline casts and renal epithelial cells. Few red and white blood cells.

*Incontinence.

	Blood		
	ERYTHROCYTE COUNT	WHITE COUNT	HEMOGLOBIN
July 8	4,100,000	29,700	75%
July 11	4,250,000	21,500	80%
July 14	.....	13,000	....
July 15	.....	13,500	....
July 18	.....	13,000	....
July 20	.....	12,700	65%
July 22	.....	10,800	....

Differential white count on July 11, 14 days after gassing.

Polynuclears	
Neutrophile	86.5 %
Eosinophile	6.75%
Basophile	.5 %
Degenerates	.75%
Lymphocytes	
Large	.25%
Small	.75%
Transitionals	.5 %
Large basophilic mononuclears	1.0 %
Myelocytes	
Neutrophile	2.5 %
Eosinophile	.25%
Myeloblasts	.25%

The polymorphonuclears are chiefly young types, showing the Arneth scale to the left. The eosinophilia is marked. The blood platelets are large and numerous. One megaloblast was found in counting four hundred white cells. No other changes in the red cells were noted.

Case III.—This patient was very severely gassed. He early developed a severe secondary infection with diffuse suppuration. There was also an extensive bronchopneumonia. After institution of active treatment by irrigation and continuous baths, the pyogenic process rapidly cleared up. Recovery after two months. The first blood count was made two weeks after gassing, and the last, four weeks after gassing.

Temperature, Pulse, and Respiration

		T.	P.	R.
June 28	A.M.	99.4	90	28
	P.M.	99.8	100	30
June 29	A.M.	100.	110	28
	P.M.	100.	110	28
June 30	A.M.	99.8	109	28 (?)
	P.M.	97.	104	28
July 1	A.M.			
	P.M.	100.8	108	26
July 2	A.M.	99.2	105	28
	P.M.	100.8	108	26
July 3	A.M.	101.	108	26
July 4	A.M.	99.6	109	18
July 5	4:00 A.M.	103.4	128	28
	4:00 P.M.	102.6	128	24
	9:00 P.M.	103.	132	30
July 6	4:00 A.M.	102.	132	26
	12:00 M.	102.	128	32
	4:00 P.M.	103.	132	28
	10:00 P.M.	102.4	120	24
July 7	2:00 A.M.	102.2	128	26

TEMPERATURE, PULSE, AND RESPIRATION (*Cont'd*)

		T.	P.	R.	
July 7	6:30 A.M.	102.6	128	26	
	12:00 M.	103.4	132	28	
	4:30 P.M.	103.4	130	28	
	10:30 P.M.	102.8	132	28	
July 8	2:00 A.M.				
	4:00 A.M.	100.4	126	28	
	8:00 A.M.	100.4	114	28	
	12:00 M.	102.2	120	28	
	4:00 P.M.	101.6	126	32	
	8:00 P.M.	102.	132	32	
	12:00 P.M.	102.2	132	28	
July 9	5:00 A.M.	101.	130	28	
	8:00 A.M.	99.8	120	26	
	12:00 M.	102.	136	32	
	4.00 P.M.	101.4	120	34	
	8:00 P.M.	101.8	130	34	(?)
	12:00 P.M.	99.8	127	34	(?)
July 10	4:30 A.M.	100.6	132	34	
	8:00 A.M.	101.6	130	32	
	12:00 M.	100.4	128	30	
	4:00 P.M.	100.4	124	26	
	8:00 P.M.	100.4	118	24	
July 11	1:00 A.M.	101.	120	24	
	4:00 A.M.	99.2	119	24	
	8:00 A.M.				
	12:00 M.	100.	128	32	
	4:00 P.M.	100.6	140	34	
	8:00 P.M.	100.8			
	12:00 P.M.	99.4	120	22	
July 12	4:00 A.M.	99.6	120	19	
	8:00 A.M.	99.8	126	20	
	12:00 M.	100.6	120	36	
	4:00 P.M.	101.2	124	34	
	8:00 P.M.	102.	124	33	
	10:00 P.M.	99.4	118	22	
July 13	12:30 A.M.	99.2	118	22	
	5:00 A.M.	99.3	124	20	
	12:00 M.	100.6	136	32	
	1:00 P.M.	101.	134	30	
	4:00 P.M.	101.	124	28	
	8:00 P.M.	100.8	125		
July 14	1:00 A.M.	100.4	120		
	4:00 A.M.	100.	124	20	
	8:00 A.M.	101.2	130	26	
	3:00 P.M.	102.2	128	20	
	4:00 P.M.	101.4	130	30	
	8:00 P.M.	100.8	120		
	11:30 P.M.	100.6	118	22	
July 15	4:00 A.M.	100.6	118	22	
	8:00 A.M.	101.5	128	32	
	12:00 M.	102.2	136	30	
	4:00 P.M.	102.2	128	28	
	8:00 P.M.	101.	125	28	
July 16	12:30 A.M.	101.	129	31	
	5:30 A.M.	100.8	125	27	
	8:00 A.M.	100.6	136	28	
	12:00 M.	100.4	124	32	
	4:00 P.M.	101.	126	28	
	8:00 P.M.	101.8	129	28	
July 17	1:00 A.M.	100.	130	26	
	5:00 A.M.	100.	132	32	
	8:00 A.M.	101.	128	30	
	12:00 M.	101.	130	28	
	4:00 P.M.	101.6	128	28	

TEMPERATURE, PULSE, AND RESPIRATION (*Cont'd*)

		T.	P.	R.
July 17	8:00 P.M.	101.	128	28
	12:00 P.M.	100.4	127	28
July 18	4:00 A.M.	99.	126	27
	8:00 A.M	100.8	130	30
	1:00 P.M.	101.3	126	28
	8:00 P.M.	101.2	130	28
	12:00 P.M.	100	134	36
July 19	4:00 A.M.	99.8	130	32
	8:00 A.M.	101.2	126	28
	12:00 M.	10.6	120	26
	4:00 P.M.	101.5	128	28
	8:30 P.M.	102.2	130	32
	11:00 P.M.	101.2	124	29
July 20	1:00 A.M.	101.4	124	28
	1:45 A.M	100.	122	30
	6:00 A.M.	100.4	124	26
	8:00 A.M.	100.6	120	22
	12:00 M.	99.8	120	20
	4:00 P.M.	101.6	128	26
	8:00 P.M.	101.8	88	24
	12:00 P.M.	100.6	128	26
July 21	4:00 A.M.	100.	128	24
	8:00 A.M.	99.8	116	22
	12:00 M.	100.6	120	26
	4:00 P.M.	101.3	124	22
	8:00 P.M.	100.8	124	24
	12:00 P.M.	100.	120	20
July 22	4:00 A.M.	100.	122	24
	8:00 A.M.	100.	120	22
	12:00 M.	100.	112	24
	4:00 P.M.	100.4	120	26
	8:00 P.M.	100.2	114	24
	12:00 P.M.	99.4	118	28
July 23	4:00 A.M.	98.3	120	26
	8:00 A.M.	100.2	116	24
	12:00 M.	99.8	124	24
	4:00 P.M.	100.	112	22
	8:00 P.M.	99.	116	30
	12:00 P.M.	99.6	120	30
July 24	4:00 A.M.	99.6	120	28
	8:00 A.M.	99.8	112	26
	12:00 M.	99.6	116	26
	4:00 P.M.	99.8	120	24
	8:00 P.M.	99.6	112	28
	12:00 P.M.	99.4	118	28
July 25	4:00 A.M.	99.8	124	22
	8:00 A.M.	101.4	124	24
	10:00 A.M.	101.8	128	24
	12:00 M.	102.	124	24
	4:00 P.M.	100.6	120	24
	8:00 P.M.	100.	120	24
	12:00 P.M.	99.6	118	24
July 26	4:00 A.M.	99.2	130	26
	8:00 A.M.	99.4	116	26
	12:00 M.	99.4	114	28
	4:00 P.M.	99.8	118	28
	8:00 P.M.	99.4	120	26
	12:00 P.M.	99.	110	22
July 27	4:00 A.M.	99.	120	22
	8:00 A.M.	99.	116	28
	12:00 M.	99.2	120	24
	4:00 P.M.	99.6	114	24
	8:00 P.M.	99.4	116	26
	12:00 P.M.	99.2	118	26
July 28	4:00 A.M.	98.6	120	20
	8:00 A.M.	99.	108	22
	12:00 M.	99.4	116	26

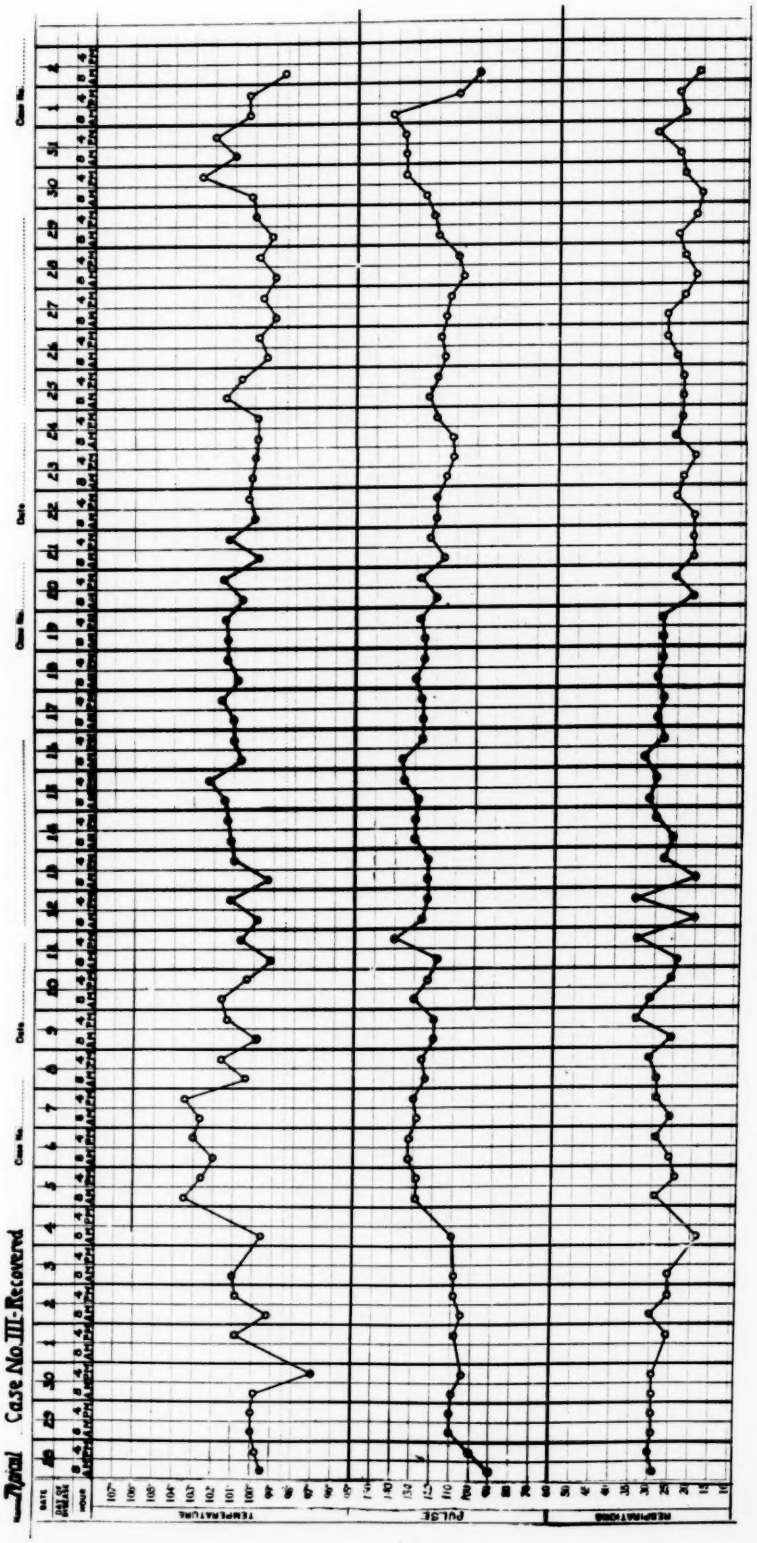
Trial Case No. III-Recovered
Case No.
Date
TEMPERATURE
PULSE
RESPIRATIONS

Chart I.

TEMPERATURE, PULSE, AND RESPIRATION (*Cont'd*)

		T.	P.	R.
July 28	4:00 P.M.	99.8	110	24
	8:00 P.M.	99.4	120	20
	12:00 P.M.	99.4	116	22
July 29	4:00 A.M.	99.4	122	26
	8:00 A.M.	99.2	120	26
	12:00 M.	99.6	114	24
	4:00 P.M.			
	8:00 P.M.	100.	122	22
	12:00 P.M.	100.4	124	26
July 30	4:00 A.M.	99.4	110	22
	8:00 A.M.	100.2	126	20
	12:00 M.	101.6	132	24
	4:00 P.M.	102.6	136	24
	8:00 P.M.	101.8	136	28
	12:00 P.M.	100.4	136	28
July 31	4:00 A.M.	100.4	136	28
	8:00 A.M.	101.	136	26
	12:00 M.	101.6	130	32
	4:00 P.M.	102.	136	32
	7:00 P.M.	101.8	136	26
	8:00 P.M.	101.6	138	26
	12:00 P.M.	100.2	120	24
Aug. 1	4:00 A.M.	100.2	136	30
	8:00 A.M.	100.2	132	24
	12:00 M.	100.	118	22
	4:00 P.M.	100.2	110	26
	8:00 P.M.	99.6	110	24
	12:00 P.M.	98.6	100	22
Aug. 2	4:00 A.M.	98.6	100	24
	6:00 A.M.	98.6	100	26
	8:00 A.M.	98.6	100	22

(For graphic chart of temperature, pulse and respiration see Chart I.)

The further recovery was uneventful. The patient was discharged as completely cured about a month later.

BLOOD

	ERYTHROCYTE COUNT	WHITE COUNT	HEMOGLOBIN
July 10	4,650,000	24,600	75%
July 12	4,800,000	21,500	75%
July 14	.....	20,000	75%
July 16	.....	15,000	....
July 18	.....	15,000	....
July 20	.....	16,000	....
July 22	.....	15,700	....
July 24	.....	15,400	....
July 26	.....	15,500	....

Differential white counts two weeks, and four weeks after gassing.

	July 11	July 25
Polynuclears		
Neutrophile	86%	79.5%
Eosinophile	7%	2.0%
Basophiles	....	1.5%
Lymphocytes		
Large	....	1.0%
Small	1%	8.5%
Transitionals	....	.5%
Large basophilic mononuclears	2%	3.5%
Myelocytes, neutrophilic,	4%	3.5%

The platelets were increased, particularly in the earlier smears. There is an increase in the large deeply staining mononuclears. The red cells show no change and no nucleated red cells were found.

Urine and Blood Urea

		PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE			SUGAR GLUCOSE	ALBUMIN	ACIDOSIS DIACETIC ACID		RENAL FUNCTIONAL EFFICIENCY				DIAZO SUB.		PIGMENTS		
DATE	FLUID INTAKE	URINE OUTPUT AMT. IN 24 HRS.	REACTION	SPECIFIC GRAVITY	FEHLING'S SOL.	HELLER'S HNO_3 RING TEST	ACETIC AC. FERROCYANIDE	FERRIC CHLORIDE	QUANT. UREA GM. PER 100 C.C.	QUANT. CHLORIDE GM. PER 100 C.C.	UREA OUTPUT IN 24 HRS.	CHLORIDE OUTPUT IN 24 HRS.	SULPHANILIC AC. EHRLICH'S DIAZO	DIMETHYLAMINOBENZALDEHYDE UROBILINOGEN	BROMIN WATER MELANIN	GMELIN'S TEST FOR BILE	FOAM TEST FOR BILE
July		c.c.									G						
8		1275	Acid	1025	Neg.	Pos.	Pos.	Neg.	—	0.06	—	0.765	—	—	—	Neg.	Neg.
9		1170	"	1025	Neg.	Pos.	Pos.	Neg.	—	0.48	—	5.6	—	—	—	Neg.	Neg.
10		1000	"	1025	Neg.	Pos.	Pos.	Neg.	0.40	0.10	4.00	1.0	—	—	—	Neg.	Neg.
11		1050	"	1017	Neg.	Pos.	Pos.	Neg.	—	0.10	—	1.05	Neg.	—	Neg.	Neg.	Neg.
FLUIDS FORCED																	
12		1870	"	1015	Neg.	Pos.	—	Neg.	0.59	0.06	—	1.12	Neg.	—	Neg.	Neg.	Neg.
13		1950	"	1014	Neg.	Pos.	—	Neg.	0.40	—	7.8	—	Neg.	—	—	Neg.	Neg.
14		1700	Slight Acid	1017	Neg.	Pos.	—	Neg.	1.75	—	29.57	—	Neg.	Pos.	—	Neg.	Neg.
15				1015	Neg.	Pos.	—	Neg.	1.42	0.12	—	—	—	Pos.	—	Neg.	Neg.
16		550	"	1020	—	Pos.	—	—	0.52	0.12	—	—	—	Pos.	—	Neg.	Neg.
17		850	"	1027	—	Pos.	—	—	0.31	0.08	2.63	0.68	—	Pos.	—	Neg.	Neg.
18	3300	750	"	1027	—	Pos.	—	—	0.88	0.10	6.6	0.75	—	Pos.	—	Neg.	Neg.
19	2640	800	"	1025	—	Pos.	—	—	0.58	0.36	4.6	2.88	—	Pos.	—	Neg.	Neg.
20	3660	1400	"	1013	—	Pos.	—	—	—	0.20	—	2.80	—	Neg.	—	Neg.	Neg.
21	2640	1925	"	1003	—	Pos.	—	—	0.44	0.22	8.47	4.24	—	Neg.	—	Neg.	Neg.
22	3360	1650	"	1013	—	Pos.	—	—	—	0.26	—	4.29	—	Pos.	—	Neg.	Neg.
23	3360	1530	Amphoteric	1010	—	Trace	—	—	—	0.70	—	10.71	—	Neg.	—	Neg.	Neg.
24	2880	950	"	1022	—	Trace	—	—	—	0.80	—	7.6	—	—	—	—	—
25	2880	1750	"	1010	—	Trace	—	—	—	0.48	—	8.4	—	—	—	—	—
26	2640	2450	Neutral	1010	—	Trace	—	—	0.24	0.30	23.00	7.35	—	—	—	—	—
27	2160	2200	Slt. Ac.	1008	—	Trace	—	—	0.48	0.26	10.56	6.72	—	—	—	—	—
28	1920	1600	" "	1015	—	Neg.	Neg.	—	0.60	0.30			—	—	—	—	—
29	1920	2100	Neutral	1015	—	Neg.	Neg.	—	0.52	—	10.92	—	—	—	—	—	—
30	—	—	Slt. Ac.	1015	—	Trace	Trace	—	—	0.55	—	—	—	—	—	—	—
31	—	1900	" "	1012	—	Neg.	Neg.	—	—	—	—	—	—	—	—	—	—

BLOOD UREA

7/10 .060 Gm. per 100 c.c. blood.
28 .045 " " " " "

PHENOLSULPHONEPHTHALEIN

7/24 1st hr. plus 10 min. 1:00 to 2:10 50%
2nd " 2:10 to 3:10 No specimen obtainable.
Total..... 50%

At 3:30 15%.

SPUTUM

Mucopurulent, frothy, profuse in amount. More than usual number of streptococci, in chains of medium length.

CAST OF BRONCHUS

Pink flesh-like. Smears showed practically a mixed culture of rather medium short chained streptococci, Gram positive diplococci, and Gram negative large thick bacilli in chains.

	COLOR OF URINE	URINARY SEDIMENT
8	Transparent, red brown.	Very heavy shower of granular casts and peculiar split fiber casts. Leucocytes. Few red blood cells. Amorphous urates. Epithelial cells.
9	Translucent, red yellow.	
10	Lighter.	
11	Darker again.	Amorphous urates, granular casts, leucocytes and red blood cells.
FLUIDS FORCED		
12	Medium dark.	Excess amorphous urates. Uric acid. Few granular casts. Mucous cylindroids. Red blood cells.
13	" "	
14	Dark.	
15	"	
16	"	Somewhat improved. Amorphous urates. Leucocytes. Few hyaline and granular casts; renal and bladder epithelial cells.
17	"	Amorphous urates. Leucocytes, hyaline and fragments of granular casts. Red blood cells. Calcium oxalate crystals.
18	"	Abundant amorphous urates. Uric acid. Red and white blood cells. Few granular casts and epithelial cells.
19	Muddy.	Much improved. Few granular casts and epithelial cells. Few leucocytes. Bacteria.
20	Lighter.	Still improving. Amorphous urates. Few granular casts. Epithelial cells. Alkaline fermentation sediment with triple phosphates.
21	Slightly dark.	Abundant amorphous urates. Few red and white blood cells. Few granular casts and epithelial cells.
22	Darker.	Large amounts of sediment. Amorphous urates, granular epithelial cells. Few triple phosphates.
23	Lighter.	Amorphous urates. Few granular casts. Epithelial cells. Triple phosphates.
24	Normal.	Amorphous urates. Triple phosphates. Few granular epithelial cells.

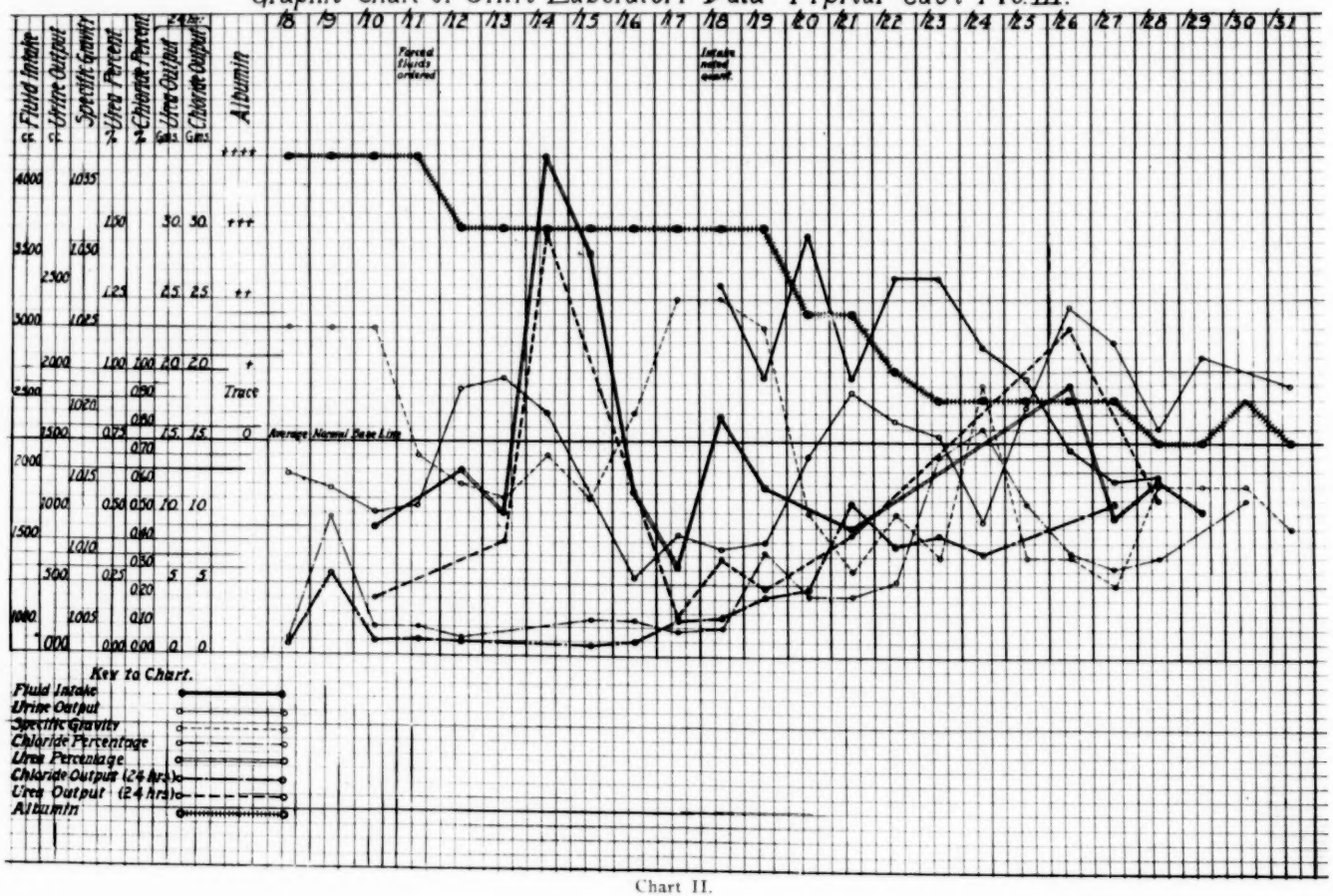
Graphic Chart of Urine Laboratory Data - Typical Case No III.
Fluid Intake c.c.
Urine Output c.c.
Specific Gravity
% Urea Percent
% Chloride Percent
Urea Output Gms.
Chloride Output Gms.
Albumin
Forced Fluids ordered
Intake reduced quickly
Average Normal Base Line
Trace
Key to Chart.
Fluid Intake
Urine Output
Specific Gravity
Chloride Percentage
Urea Percentage
Chloride Output (24 hrs.)
Urea Output (24 hrs.)
Albumin

Chart II.

URINE AND BLOOD UREA (*Cont'd*)

	COLOR	SEDIMENT
25	Slightly dark.	Amorphous urates. Uric acid. Triple phosphates. Few granular leucocytes and epithelial cells.
26	Normal.	Slight sediment. Alkaline fermentation. Triple phosphates.
27	Medium dark.	Amorphous urates and triple phosphates.
28	Normal.	Amorphous urates and triple phosphates.
29	"	Much sediment, carbonates.
30	Sl. darker.	Few amorphous urates and triple phosphates. Few granular epithelial cells.
31	Normal.	Few granular epithelial cells, few leucocytes, otherwise normal.

(For graphic chart of the urinary changes, see Chart II.)

CASE IV.—This was a rather severe case of mustard gassing. The patient had extreme nausea and vomiting for five hours during the first night after being gassed. He developed severe genital lesions which became secondarily infected. There was also necrosis of the nasal and pharyngeal mucosa and some bronchitis.

TEMPERATURE, PULSE, AND RESPIRATION

		T.	P.	R.
July 4		Normal	Normal	Normal
July 5	8:00 A.M.	98.6	96	26
	4:00 P.M.	98.2	80	
July 6	4:00 A.M.	97.	80	18
	4:00 P.M.	98.6	96	18
July 7	6:00 A.M.	97.4	82	19
	8:00 A.M.			
	4:30 P.M.	99.	100	22
July 8	8:00 A.M.	97.4	92	22
	4:00 P.M.	97.6	94	22
July 9	4:00 P.M.	98.6	102	20
July 10	8:00 A.M.	97.6	100	24
	4:00 P.M.	98.6	98	20
July 11	4:00 P.M.	99.	112	24
July 12	4:00 P.M.	99.6	106	22
July 13	4:00 P.M.	100.	116	22
July 14	4:00 P.M.	100.	109	
July 15	8:00 A.M.	98.8	112	18
	4:00 P.M.	99.8	112	28
July 16	8:00 A.M.	98.8	86	
	4:00 P.M.	98.8	92	
July 17	7:30 A.M.	98.2	98	
	4:00 P.M.	98.8	78	
July 18	7:30 A.M.	100.	98	
	4:00 P.M.	99.8	88	
July 19	8:00 A.M.	98.8	80	
	4:00 P.M.	98.8	88	
July 20	7:30 A.M.	98.6	86	
	4:00 P.M.	99.	88	
July 21	7:30 A.M.	98.4	82	
	4:00 P.M.	99.	76	
July 22	7:30 A.M.	98.2	78	
	4:00 P.M.	98.8	82	
July 23	8:00 A.M.	98.6	78	20
	4:00 P.M.	98.6	98	20
July 24	8:00 A.M.	98.	80	18
	4:00 P.M.	98.6	112	20
July 25	8:00 A.M.	98.6	86	
	4:00 P.M.	98.8	88	
July 26	8:00 A.M.	98.6	80	
	4:00 P.M.	98.8	84	
July 27	8:00 A.M.	98.4	82	
	4:00 P.M.	98.6	86	
July 28	8:00 A.M.	98.	84	20
	4:00 P.M.	98.6	98	22
July 29	8:00 A.M.	98.2	86	18
	4:00 P.M.	98.6	98	

Urine and Blood Urea

	PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE			SUGAR GLUCOSE	ALBUMIN	ACIDOSIS DIACETIC ACID	RENAL FUNCTIONAL EFFICIENCY				DIAZO SUB.	PIGMENTS			
DATE	URINE OUTPUT AMT. IN 24 HRS.	REACTION	SPECIFIC GRAVITY	FEHLING'S SOL.	HELLER'S HNO_3 RING TEST	ACETIC AC. FERROCYANIDE	FERRIC CHLORIDE	QUANT. UREA GM. PER 100 C.C.	QUANT. CHLORIDE GM. PER 100 C.C.	UREA OUTPUT IN 24 HRS.	CHLORIDE OUTPUT IN 24 HRS.	SULPHANILIC AC. EHRLICH'S DIAZO	DIMETHYLAMINOBENZALDEHYDE UROBILINOGEN	BROMIN WATER MELANIN	GMELIN'S TEST FOR BILE	FOAM TEST FOR BILE
July	c.c.									G.	G.					
8	1000	Acid	1026	Neg.	Pos.	Pos.	Neg.	—	0.14	—	1.40	—	—	—	Neg.	Neg.
9	1000	"	1030	Neg.	Pos.	Pos.	Neg.	—	0.20	—	2.00	—	—	—	Neg.	Neg.
10	1600	"	1018	Neg.	Pos.	Pos.	Neg.	0.36	0.32	5.76	5.12	—	—	—	Neg.	Neg.
11	525	"	1023	Neg.	Pos.	Pos.	Neg.	—	0.26	—	1.36	Neg.	—	Neg.	Neg.	Neg.
12	1025	"	1020	Neg.	Pos.		Neg.	0.68	0.26	6.97	2.67	Neg.	—	Neg.	Neg.	Neg.
13	1600	"	1013	Neg.	Pos.		Neg.	0.62	—	9.92	—	Neg.	—	—	Neg.	Neg.
14	1100	Amphoteric	1027	Neg.	Pos.		Neg.	2.56	—	28.16	—	Neg.	—	Neg.	Neg.	Neg.
15		Neutral	1015	—	Pos.		Neg.	1.22	0.20	—	—	—	Neg.	—	Neg.	Neg.
16	NO SPECIMEN COLLECTED															
17	350	Acid	1023	—	Pos.		Neg.	—	0.30	—	1.05	—	Neg.	—	Neg.	Neg.
18	1150	Neutral	1015	—	Pos.		—	0.67	0.80	7.60	9.20	—	Neg.	—	Neg.	Neg.
19	450?	Acid	1020	—	Neg.	Neg.	—	0.24	0.60	1.08	2.70	—	Neg.	—	Neg.	Neg.
20	650	"	1017	—	Neg.	Neg.	—	—	0.26	—	1.69					
21	540	"	1022	—	Pos.	Pos.	—	—	0.60	—	3.24	—	Neg.	—	Neg.	Neg.
22	1100	"	1019	—	Pos.	Pos.	—	—	0.58	—	6.38	—	Neg.	—	Neg.	Neg.
23	1075	Slight	1015	—	Neg.	Neg.	—	—	0.48	—	5.16	—	—	—	—	—
24	1000	"	1022	—	Neg.	Neg.	—	—	0.50	—	5.00	—	—	—	—	—
25	625	"	1017	—	Neg.	Neg.	—	—	0.58	—	3.62	—	—	—	—	—
26	1200	"	1022	—	Neg.	Neg.	—	1.05	0.58	1.80	6.96	—	—	—	—	—
27	800	"	1025	—	Pos.	Pos.	—	0.74	0.46	5.92	3.68	—	—	—	—	—
28	300	"	1023	—	Neg.	Neg.	—	0.72	0.66	2.16	1.98	—	—	—	—	—
29	500	"	1022	—	Neg.	Neg.	—	0.52	—	2.60	—	—	—	—	—	—

BLOOD UREA

10 .0480 gm. per 100 c.c.

PHENOLSULPHONEPHTHALEIN TEST

July 24 1st hr. plus 10 min. 9:30 to 10:40 — 80
10:40 to 11:40 — 10
Total.....90

	COLOR OF URINE	URINARY SEDIMENT
	Medium lemon yellow.	
8	Turbid, heavy deposit.	Uric acid. Amorphous urates, crystals in showers. Cylindroids. Few granular casts. Epithelial cells.
9	Medium yellow, translucent.	
10	Straw color. Slightly turbid.	
11	Darker. Turbid.	Uric acid and amorphous urates in great showers. Few granular casts. Few white and red blood cells, few epithelial cells.
12	Normal.	Uric acid and amorphous urates. Otherwise negative.
13	Turbid.	
14	Dirty yellow.	
15	Normal.	
16	NO SPECIMEN COLLECTED.	
17	Medium dark, turbid.	Few uric acid and amorphous urates. Few triple phosphates and calcium oxalate. Few hyaline casts, renal and urethral epithelial cells. Numerous leucocytes.
18	Slightly dark, translucent.	Abundant uric acid and urates. Few triple phosphates, few granular epithelial casts.
19	Normal sediment.	Almost entirely amorphous urates. Few uric acid and few triple phosphates.
20	Normal.	Abundant amorphous urates, few uric acid, triple phosphates. Granular casts and granular epithelium.
21	Normal.	As above.
22	Normal.	As above but no casts noted.
23	Somewhat pale.	As above but no casts noted.
24	Normal.	As above but no casts noted.
25	Normal.	As above but no casts noted.
26	Normal.	Only triple phosphates and a few epithelial cells.
27	Medium dark.	As above.
28	Normal.	As above.
29	Normal.	Amorphous urates. Uric acid. Numerous leucocytes. Triple phosphates.

BLOOD

Examination of blood two weeks after gassing.

Erythrocyte count		4,500,000
White count		25,000,
Hemoglobin		76%
Differential white count:		
Polynuclears		
Neutrophile	84.0%	
Eosinophile	1.5%	
Lymphocytes		
Large	2.0%	
Small	3.0%	
Transitionals	.5%	
Large basophilic mononuclears	1.5%	
Myelocytes, neutrophilic,	7.5%	

The blood platelets were increased. There were no changes in the red cells.

CASE V.—This patient had severe mustard gas burns about the genitals, in the axillæ and at the bends of the elbows. There was a less severe generalized burn. A marked generalized secondary furunculosis complicated the later course of this patient.

TEMPERATURE, PULSE, AND RESPIRATION

		T.	P.	R.
June 27	7:30 P.M.	97.6	112	26
June 28		98.2	110	24
June 29				
June 30		98.6	90	
July 1		99.	82	
July 2		98.8	90	
July 3	5:00 P.M.	98.8	97	
July 4	6:00 A.M.	98.4	110	
July 5	4:00 P.M.	100.	108	
July 6	4:00 A.M.	98.	102	22
	4:00 P.M.	99.2	116	22
July 7	4:00 A.M.	98.	108	22
	4:00 P.M.	98.6	104	22
July 8	2:45 A.M.			
	4:00 A.M.	97.	110	
	4:00 P.M.	99.6	112	18
July 9	4:00 A.M.	98.8	98	20
July 10	8:00 A.M.	96.8	112	16
	4:00 P.M.	99.4	112	24
July 11	4:00 P.M.	99.	110	22
July 12	4:00 P.M.	99.4	106	22
July 13	4:00 P.M.	100.6	102	20
July 14	7:30 P.M.	102.	110	
July 15	8:00 A.M.	99.	100	18
	12:00 M.	98.8	100	18
	4:00 P.M.	100.	112	26
	7:30 P.M.			
July 16	8:00 A.M.	98.6	88	
	4:00 P.M.	98.6	92	
July 17	7:30 A.M.	98.2	88	
	4:00 P.M.	98.	82	
July 18	7:30 A.M.	98.2	88	
	4:00 P.M.	98.2	84	
July 19	8:00 A.M.	97.8	80	
	4:00 P.M.	98.	78	
July 20	7:30 A.M.	97.6	68	
	4:00 P.M.	98.4	76	
July 21	8:00 A.M.			
	4.00 P.M.	98.8	78	

TEMPERATURE, PULSE, AND RESPIRATION (*Cont'd*)

		T.	P.	R.
July 22	7:30 A.M.	97.8	76	
	4:00 P.M.	98.6	80	
July 23	8:00 A.M.	98.	68	
	4:00 P.M.	98.2	76	
July 24	8:00 A.M.	97.	74	
	4:00 P.M.	98.6	82	
July 25	8:00 A.M.	97.6	68	
	4:00 P.M.	99.	78	
July 26	8:00 A.M.	97.8	78	
	4:00 P.M.	98.8	78	
July 27	8:00 A.M.	98.	76	
	4:00 P.M.	98.6	78	
July 28	8:00 A.M.	97.4	70	18
July 29	8:00 A.M.	98.2	68	18
	4:00 P.M.	98.	80	20

URINE AND BLOOD UREA

	PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE			SUGAR GLUCOSE	ALBUMIN		ACIDOSIS DIACETIC ACID	RENAL FUNCTIONAL EFFICIENCY				DIAZO SUB.	PIGMENTS			
DATE	URINE OUTPUT AMT. IN 24 HRS.	REACTION	SPECIFIC GRAVITY	FEHLING'S SOL.	HELLER'S HNO_3 RING TEST	ACETIC AC. FERROCYANIDE	FERRIC CHLORIDE	QUANT. UREA GM. PER 100 C.C.	QUANT. CHLORIDE GM. PER 100 C.C.	UREA OUTPUT IN 24 HRS.	CHLORIDE OUTPUT IN 24 HRS.	SULPHANILIC AC. EHRLICH'S DIAZO	DIMETHYLAMINOBENZALDEHYDE UROBILINOGEN	BROMIN WATER MELANIN	GMELIN'S TEST FOR BILE	FOAM TEST FOR BILE
July	c.c.															
8	1350	Acid	1026	Neg.	Pos.	Pos.	Neg.	—	0.56	—	7.56	—	—	—	Neg.	Neg.
9	500	"	1026	Neg.	Pos.	Pos.	Neg.	—	0.64	—	3.20	—	—	—	Neg.	Neg.
10	950	"	1022	Neg.	Pos.	Pos.	Neg.	0.49	0.28	4.65	7.66	—	—	—	Neg.	Neg.
11	600	"	1022	Neg.	Pos.	Pos.	Neg.	—	0.66	—	0.36	Neg.	—	Neg.	Neg.	Neg.
12	900	Slight	1018	Neg.	Pos.	Pos.	Neg.	0.40	0.30	3.60	2.70	Neg.	—	Neg.	Neg.	Neg.
13	970	Acid	1020	Neg.	Pos.	Pos.	Neg.	0.73	—	7.08	—	—	—	—	Neg.	Neg.
14	850	"	1025	Neg.	Pos.	Pos.	Neg.	1.26	—	10.71	—	Neg.	—	Neg.	Neg.	Neg.
15	—	Slight	1025	Neg.	Trace	—	Neg.	1.61	0.34	—	—	—	—	—	Neg.	Neg.
16	675	Acid	1015	Neg.	Pos.	—	Neg.	0.40	0.34	2.70	2.30	—	—	Neg.	Neg.	Neg.
17	1425	"	1013	Neg.	Trace	—	Neg.	—	0.52	—	7.41	—	Neg.	—	Neg.	Neg.
18	700	"	1023		Neg.	Neg.	Neg.	0.44	0.78	3.08	5.46	—	Neg.	—	Neg.	Neg.
19	750	"	1025	—	Neg.	Neg.	—	0.52	0.86	3.90	6.54	—	Neg.	—	Neg.	Neg.
20	1100	"	1010	—	Neg.	—	—	—	0.38	—	4.18	—	Neg.	—	Neg.	Neg.
21	620	"	1024	—	Neg.	—	—	—	0.48	—	2.97	—	—	—	Neg.	Neg.
22	1100	"	1010	—	Neg.	—	—	—	0.62	—	6.82	—	Neg.	—	Neg.	Neg.
23	1625	"	1010	—	Neg.	—	—	—	0.54	—	8.77	—	—	—	Neg.	Neg.
24	1400	"	1012	—	Neg.	—	—	—	0.72	—	10.08	—	—	—	Neg.	Neg.
25	1000	"	1010	—	Neg.	—	—	—	0.76	—	7.60	—	—	—	Neg.	Neg.
26	2100	"	1013	—	Neg.	—	—	0.72	0.60	15.12	12.60	—	—	—	Neg.	Neg.
27	1600	Slight	1015	—	Neg.	—	—	0.67	0.60	10.72	9.60	—	—	—	Neg.	Neg.
28	2000	"	1015	—	Neg.	—	—	0.50	0.50	10.00	10.00	—	—	—	Neg.	Neg.
29	1400	"	1015	—	—	—	—	—	—	—	—	—	—	—	—	—

BLOOD UREA

Blood unobtainable.

PHENOLSULPHONEPHTHALEIN TEST

July 24 1st hour plus 10 min. 70% excreted.
2nd hour 15% "

Total.....85%

Smears from furuncles and hordeolum showed only pus and staphylococci.

COLOR OF URINE

8 Medium lemon yellow, cloudy.
9 Medium lemon yellow, translucent.
11 Darker.
12
13 Medium dark.
14 Dark.

URINARY SEDIMENT

Uric acid and amorphous urates. Few casts and cylindroids, granular and hyaline casts, epithelial squamous cells with large golden yellow droplets, markedly refractive. Fatty degeneration.

As above plus calcium oxalate crystals. Fragments of granular casts.
As above. Crystals in excess. Few red blood cells, few leucocytes, few granular casts.

URINE AND BLOOD UREA (*Cont'd*)

	COLOR OF URINE	URINARY SEDIMENT
15	Normal.	Sediment much improved.
16	Medium dark.	Few fragments of granular casts. Epithelial cells, leucocytes and amorphous urates.
17	Pale.	As above plus few red blood cells.
18	Normal	Uric acid, amorphous urates, calcium oxalate. Few red and white blood cells. Few granular epithelial cells.
19	Normal.	Abundant uric acid, as above.
20	Normal.	As above.
21	Slightly pale.	As above.
22	Normal.	As above.
23	Slightly pale.	As above and a few granular casts.
24	Slightly pale.	As above.
25	Normal.	Improved, only a few urates and a few granular epithelial cells were found.
26	Pale.	As next above.
27	Pale.	As next above.
28	Normal.	As next above.
29	Normal.	As next above.

BLOOD

Examination of blood sixteen days after gassing.

Erythrocyte count		4,600,000
White count		21,200
Hemoglobin		78%
Differential white count:		
Polynuclears		
Neutrophile	92. %	
Eosinophile	1.5%	
Basophile	.5%	
Lymphocytes		
Large	2.0%	
Small	2.0%	
Transitionals	1.0%	
Large mononuclears, none found		
Myelocytes	1.0%	

The polymorphonuclears show the Arneth scale to the right, older polynuclears. The platelets are greatly increased in number. Many of the red cells are undersized. No nucleated red cells were found.

CASE VI.—In this case there were severe genital burns which developed a severe secondary pyogenic infection. The general skin involvement was less severe, but well marked.

BLOOD

Examination of blood two weeks after gassing.

Erythrocyte count		4,860,000
White count		16,600
Hemoglobin		78%
Differential white count:		
Polynuclears		
Neutrophile	66 %	
Eosinophile	4.5%	
Lymphocytes		
Large	3.0%	
Small	7.5%	
Transitionals	1.5%	
Large basophilic mononuclears	5.5%	
Myelocytes	12.0%	

The blood platelets are increased. There are no changes in the red cells. No nucleated red cells were found.

URINE AND BLOOD UREA

	PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE			SUGAR GLUCOSE	ALBUMIN		ACIDOSIS DIACETIC ACID	RENAL FUNCTIONAL EFFICIENCY				DIAZO SUB.		PIGMENTS		
DATE	URINE OUTPUT AMT. IN 24 HRS.	REACTION	SPECIFIC GRAVITY	FEHLING'S SOL.	HELLER'S HNO_3 RING TEST	ACETIC AC. FERROCYANIDE	FERRIC CHLORIDE	QUANT. UREA GM. PER 100 C.C.	QUANT. CHLORIDE GM. PER 100 C.C.	UREA OUTPUT IN 24 HRS.	CHLORIDE OUTPUT IN 24 HRS.	SULPHANILIC AC. EHRLICH'S DIAZO	DIMETHYLAMINOBENZALDEHYDE UROBILINOGEN	BROMIN WATER MELANIN	GMELIN'S TEST FOR BILE	FOAM TEST FOR BILE
July	c.c.															
8	460	Acid	1024	Neg.	Pos.	Pos.	Neg.	—	0.16	—	0.82	Neg.	—	Neg.	Neg.	Neg.
9	750	"	1015	Neg.	Pos.	Pos.	Neg.	—	0.30	—	2.25	—	—	—	Neg.	Neg.
10	1150	"	1015	Neg.	Pos.	Pos.	Neg.	0.38	0.14	4.38	1.61	Neg.	—	Neg.	Neg.	Neg.
11	620	Mark	1024	Neg.	Pos.	Pos.	Neg.	—	0.38	—	7.45	—	—	—	Neg.	Neg.
12	630	Acid	1024	Neg.	Trace	Trace	Neg.	0.58	1.16	3.65	7.31	—	—	—	Neg.	Neg.
13	300?	"	1018	Neg.	Trace	Trace	Neg.	0.36	—	1.08	—	—	—	—	Neg.	Neg.
14	900	"	1020	Neg.	Pos.	Pos.	Neg.	1.56	—	14.04	—	Neg.	—	Neg.	Neg.	Neg.
15	NO SAMPLE															
16	NO SAMPLE															
17	1600	Acid	1018	Neg.	Pos.	Pos.	Neg.	—	0.40	—	6.40				Neg.	Neg.
18	LEFT THE INFIRMARY.															

	BLOOD UREA	PHENOLSULPHONEPHTHALEIN TEST
	Blood unobtainable.	Patient left before the apparatus was secured.
	COLOR OF URINE	URINARY SEDIMENT
8	Turbid. Deep lemon yellow.	Amorphous urates and uric acid crystals in showers. Few leucocytes. Few hyaline casts.
9	Light lemon, cloudy.	
10	Lighter.	
11	Darker again.	As above plus calcium oxalate crystals, in great numbers. Granular as well as hyaline casts. Epithelial cells, both renal and bladder.
12	Normal.	As above except no casts were noted.
13	Normal.	
14	Lighter, normal.	
15	Normal.	
16	Normal.	
17	Normal.	Few uric acid and amorphous urates. Few fragments of granular casts. Few
18	Normal.	red and white blood cells.

CASE VII.—Comparatively mild case of mustard gassing. Slight burns of genitals, axillæ and in the bends of the elbows. General erythema of skin over entire body.

BLOOD

Examination of blood two weeks after gassing.

Erythrocyte count		5,300,000
White count		19,500
Hemoglobin		100%
Differential white count		
Polynuclears		
Neutrophiles	71.5%	
Eosinophiles	5.5%	
Lymphocytes		
Large	3.5%	
Small	10.5%	
Transitionals	.5%	
Large basophilic mononuclears	6.0%	
Myelocytes	2.5%	

There is an increase in the normal granular mononuclears. The blood platelets are increased. No nucleated reds, or other changes in the red cells, were found.

Urine and Blood Urea

	PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE			SUGAR GLUCOSE	ALBUMIN		ACIDOSIS DIACETIC ACID	RENAL FUNCTIONAL EFFICIENCY				DIAZO SUB.		PIGMENTS		
DATE	URINE OUTPUT AMT. IN 24 HRS.	REACTION	SPECIFIC GRAVITY	FEHLING'S SOL.	HELLER'S HNO_3 RING TEST	ACETIC AC. FERROCYANIDE	FERRIC CHLORIDE	QUANT. UREA GM. PER 100 C.C.	QUANT. CHLORIDE GM. PER 100 C.C.	UREA OUTPUT IN 24 HRS.	CHLORIDE OUTPUT IN 24 HRS.	SULPHANILIC AC. EHRLICH'S DIAZO	DIMETHYLAMINOBENZALDEHYDE UROBILINOGEN	BROMIN WATER MELANIN	GMELIN'S TEST FOR BILE	FOAM TEST FOR BILE
July	c.c.															
8	575	Acid	1026	Neg.	Pos.?	Pos.?	Neg.	—	0.82	—	4.62	—	—	—	Neg.	Neg.
9	1000	"	1027	Neg.	Pos.	Pos.	Neg.	—	.0.52	—	5.20	—	—	—	Neg.	Neg.
10	1000	"	1027	Neg.	Pos.?	Pos.?	Neg.	0.38	0.14	3.80	1.40	—	—	—	Neg.	Neg.
11	900	"	1020		Pos.	Pos.	Neg.	—	0.12	—	1.08	Neg.	—	Neg.	Neg.	Neg.
12	1450	"	1019	Neg.	Neg.	Neg.	Neg.	0.54	0.34	7.83	4.93	Neg.	—	Neg.	Neg.	Neg.
13	250?	"	1027	Neg.	Pos.	Pos.		1.12	—	2.80?	—	Neg.	—	Neg.	Neg.	Neg.
14	600	"	1025	Neg.	Pos.	Pos.	Neg.	2.26	—	13.56	—	Neg.	—	Neg.	Neg.	Neg.
15	—	"	1025	Neg.	Neg.	Neg.	Neg.	1.32	0.80	—	—	—	Neg.	—	Neg.	Neg.
16	NO SAMPLE															
17	400?	"	1023		Neg.	—	Neg.	—	0.52	—	2.08?	—	Neg.	—	Neg.	Neg.
18	900	Neut.	1025		Pos.	Pos.	Neg.	0.48	0.54	4.32	4.86	—	Neg.	—	Neg.	Neg.
19	600	Acid	1025		Neg.	Neg.		0.48	0.86	2.88	4.56	—	Neg.	—	Neg.	Neg.
20	550	"	1025		Neg.	Neg.	—	—	0.30	—	1.65	—	Neg.	—	Neg.	Neg.
21	590	"	1027		Trace	Trace	—	—	0.20	—	1.18	—	Neg.	—	Neg.	Neg.
22	900	"	1017		Trace	Trace	—	—	0.38	—	3.42	—	Neg.	—	Neg.	Neg.
23	565	"	1024		Neg.	Neg.	—	—	0.70	—	4.65	—	Neg.	—	Neg.	Neg.
24	500	"	1025		Neg.	Neg.	—	—	0.72	—	3.60	—	—	—	Neg.	Neg.
25	LEFT THE HOSPITAL.															

BLOOD UREA

July 10 .0264 Gm. per 1000 c.c. of blood

PHENOLSULPHONEPHTHALEIN

1st hr. plus 10 min. 60% excreted.
2nd hr. 20% "

Total.....80% "

URINARY SEDIMENT

8 Few amorphous urates and uric acid crystals. Few cylindroids and granular casts. Few epithelial cells.

11 Amorphous urates. Few uric acid crystals and calcium oxalate crystals. Few hyaline and granular casts and cylindroids. Leucocytes and a few red blood cells and epithelial cells.

12 Few amorphous urates. Few squamous epithelial cells, otherwise normal.

17 Abundant amorphous urates, few uric acid crystals. Few leucocytes and granular epithelial cells.

18 Sediment crystalline in character. Abundant uric acid and urates, numerous calcium oxalate crystals. Few leucocytes and granular epithelial cells.

19 Few amorphous urates and uric acid and calcium oxalate crystals.

20 Abundant amorphous urates, uric acid and calcium oxalate. Triple phosphates. Few leucocytes. Few granular epithelial cells.

21 Few amorphous urates, uric acid, calcium oxalate; few hyaline and few fragments of blood casts. Few granular epithelial cells.

22 Amorphous urates. Few calcium oxalates and triple phosphates.

23 Excess of amorphous urates and triple phosphates, otherwise negative.

Case VIII.—Mild case. Recovery.

Urine and Blood Urea

	PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE			SUGAR GLUCOSE	ALBUMIN	ACIDOSIS DIACETIC ACID		RENAL FUNCTIONAL EFFICIENCY				DIAZO SUB.		PIGMENTS		
DATE	URINE OUTPUT AMT. IN 24 HRS.	REACTION	SPECIFIC GRAVITY	FEHLING'S SOL.	HELLER'S HNO3 RING TEST	ACETIC AC. FERROCYANIDE	FERRIC CHLORIDE	QUANT. UREA GM. PER 100 C.C.	QUANT. CHLORIDE GM. PER 100 C.C.	UREA OUTPUT IN 24 HRS.	CHLORIDE OUTPUT IN 24 HRS.	SULPHANILIC AC. EHRLICH'S DIAZO	DIMETHYLAMINOBENZALDEHYDE UROBILINOGEN	BROMIN WATER MELANIN	GMELIN'S TEST FOR BILE	FOAM TEST FOR BILE
July	c.c.															
8	585?	Acid	1030	Neg.	Pos.?	Pos.	Neg.	—	0.22	—	1.28	—	—	—	Neg.	Neg.
9	450?	"	1025	Neg.	Pos.	Pos.	Neg.	—	0.22	—	.99	—	—	—	Neg.	Neg.
10	950	"	1017	Neg.	Pos.	Pos.	Neg.	0.25	0.36	2.37	3.42	—	—	—	Neg.	Neg.
11	500?	"	1023		Pos.	Pos.	Neg.	—	0.40	—	2.00	Neg.	—	Neg.	Neg.	Neg.
12	1125	"	1015	Neg.	Trace	Trace	Neg.	0.43	0.38	4.83	4.27	Neg.	—	Neg.	Neg.	Neg.
13	—	"		Neg.				0.78	—	—	—					
14	920	Alk.	1025	Neg.	Pos.	Pos.	Neg.	0.12	—	1.10	—	Neg.	—	Neg.	Neg.	Neg.
15	NO SAMPLES SUBMITTED AFTER THE ABOVE EXAMINATIONS.															

BLOOD UREA. .0312 G per 100 c.c. NO FURTHER DATA OBTAINABLE.

URINARY SEDIMENT

8 Calcium oxalate crystals. Few granular casts and cylindroids. Epithelial cells and leucocytes.

11 Amorphous urates. Small granular casts. Many epithelial cells (renal and bladder type). Few red and white blood cells.

12 Excess of amorphous urates, few uric acid, few granular casts. Red blood cells? Granular bladder epithelial cells.

Blood

Hemoglobin. 75 per cent. No other examination made.

Case IX.—Mild case. Recovery.

Temperature, Pulse, and Respiration

		T.	P.	R.
July 11		Normal		
July 12		Normal		
July 13		Normal		
	4:00 P.M.	97.6	76	
July 14		Normal		
July 15		Normal		
July 16	8:30 A.M.	98.4	78	
	4:00 P.M.	98.8	80	
July 17	7:30 A.M.	98.	76	
	4:00 P.M.	98.6	88	
July 18	7:30 A.M.	98.2	78	
	4:00 P.M.	98.2	74	
July 19	8:00 A.M.	98.	78	
	4:00 P.M.	98.4	79	
July 20	7:30 A.M.	98.	76	
	4:00 P.M.	98.6	80	
July 21	7:30 A.M.	97.8	70	
July 22	7:30 A.M.	98.	80	
	4:00 P.M.	98.6	82	

Temperature, Pulse, and Respiration (*Cont'd*)

		T.	P.	R.
July 23	8:00 A.M.	98.	68	
	4:00 P.M.	98.	80	18
July 24	8:00 A.M.	98.	80	18
	4:00 P.M.		84	20
July 25	8:00 A.M.	98.	76	18
	4:00 P.M.	98.6	82	
July 26	8:00 A.M.	98.	78	
	4:00 P.M.	98.	82	
July 27	8:00 A.M.	98.	80	
	4:00 P.M.	98.6	80	
July 28	8:00 A.M.	97.8	76	
	4:00 P.M.	98.6	76	
July 29	8:00 A.M.			
	4:00 P.M.	98.4	74	

Urine and Blood Urea

	PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE			SUGAR GLUCOSE	ALBUMIN	ACIDOSIS DIACETIC ACID		RENAL FUNCTIONAL EFFICIENCY				DIAZO SUB.	PIGMENTS			
DATE	URINE OUTPUT AMT. IN 24 HRS.	REACTION	SPECIFIC GRAVITY	FEHLING'S SOL.	HELLER'S HNO$_3$ RING TEST	ACETIC AC. FERROCYANIDE	FERRIC CHLORIDE	QUANT. UREA GM. PER 100 C.C.	QUANT. CHLORIDE GM. PER 100 C.C.	UREA OUTPUT IN 24 HRS.	CHLORIDE OUTPUT IN 24 HRS.	SULPHANILIC AC. EHRLICH'S DIAZO	DIMETHYLAMINOBENZALDEHYDE UROBILINOGEN	BROMIN WATER MELANIN	GMELIN'S TEST FOR BILE	FOAM TEST FOR BILE
July	c.c.															
17	550	Acid	1024	Neg.	Neg.	Neg.	Neg.	—	0.58	—	3.19	Neg.	Neg.	Neg.	Neg.	Neg.
18	650	"	1018	Neg.	Neg.	Neg.	Neg.	0.49	0.70	3.18	4.55	—	Neg.	—	Neg.	Neg.
19	1100	"	1015	Neg.	Neg.	Neg.	Neg.	0.32	0.60	3.52	6.60	—	Neg.	—	Neg.	Neg.
21	1050	"	1015	—	Neg.	Neg.	Neg.	—	0.78	—	8.19	—	Neg.	—	Neg.	Neg.
22	500	Neut.	1017	—	Neg.	Neg.	Neg.	—	0.58	—	2.90	—	Neg.	—	Neg.	Neg.
23	820	"	1017	—	Neg.	Neg.	Neg.	—	0.34	—	2.78	—	—	—	—	—
24	1850	Acid	1012	—	Neg.	Neg.	Neg.	—	0.70	—	12.95	—	—	—	—	—
25	1150	"	1013	—	Neg.	Neg.	Neg.	—	0.38	—	4.37	—	—	—	—	—
26	700		1025	—	Neg.	Neg.	Neg.	1.6	0.36	11.20	2.52	—	—	—	—	—
27	1050		1015		Neg.	Neg.		0.72	0.70	7.56	7.35	—	—	—	—	—
28	400?	Acid	1023		Neg.	Neg.		0.84	0.66	3.33	2.64	—	—	—	—	—
29	700	"	1017		Neg.	Neg.		—	—	—	—	—	—	—	—	—

PHENOLSULPHONEPHTHALEIN TEST

1st hr. plus 10 min. 60% excreted.
2nd hr. 10% "
Total..... 70% "

URINARY SEDIMENT

17 Few amorphous urates, few leucocytes, few red and white blood cells, few granular epithelial cells.
18 Crystalline in character consisting largely of uric acid and amorphous urates. Otherwise normal.
19 Excess of uric acid and amorphous urates. Otherwise negative.
21 Abundant amorphous urates. Otherwise negative.
22 Crystalline. Large amounts amorphous urates. Some triple phosphates, otherwise negative.
23 As on previous day, less in amount.
24 As on previous day, still less in amount.
25 Excess amorphous urates, triple phosphates, otherwise negative.
26 As next above.

Case Group X.—All mild cases with recovery.

Temperature, Pulse, and Respiration

CASE X-A

		T.	P.	R.
July 27	8:00 A.M.	97.8	68	
	4:00 P.M.	98.4	74	
July 28	8:00 A.M.	97.8	68	
	4:00 P.M.	98.8	76	20
July 29	8:00 A.M.	97.	68	18
	4:00 P.M.	98.2	80	

CASE X-B

July 22	7:30 A.M.	97.8	78	
	4:00 P.M.	98.4	80	
July 23	8:00 A.M.	97.6	72	
July 24	8:00 A.M.	97.	76	
	4:00 P.M.	98.6	78	
July 25	8:00 A.M.	97.6	78	
	4:00 P.M.	98.6	78	
July 27	8:00 A.M.	98.4	74	
July 28	8:00 A.M.	97.	68	
July 29	8:00 A.M.	Normal		
	4:00 P.M.	98.	76	

CASE X-C

July 23	10:00 P.M.	97.6	70	19
July 24	8:00 A.M.	97.6	74	20
	4:00 P.M.	98.2	76	20
July 25	8:00 A.M.	98.	74	18
	4:00 P.M.	98.	74	
July 26	8:00 A.M.	97.8	74	
	4:00 P.M.	98.	76	
July 27	8:00 A.M.	97.8	74	
	4:00 P.M.	98.4	74	
July 28	8:00 A.M.	97.4	76	18
	4:00 P.M.	98.6	80	20
July 29	8:00 A.M.	97.6	76.	
	4:00 P.M.	98.2		

CASE X-D

Normal Normal Normal

Urine and Blood Urea

	PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE				ALBUMIN					
	REACTION	SPECIFIC GRAVITY	FEHLING'S SOL.	HELLER'S HNO_3 RING TEST	ACETIC AC. FERROCYANIDE	HEAT AND NITRIC ACID	HEAT AND ACETIC ACID	PER CENT CHLORIDE GM. PER 100 C.C.	COLOR	SEDIMENT
A.*	Acid	1022	Neg.	Neg.	Neg.	Neg.	Neg.	0.38	Clear Normal.	Negative.
B.**	"	1020	Neg.	Neg.	Neg.	Neg.	Neg.	0.54	Clear-Normal.	Negative.
C.***	"	1020	Neg.	Neg.	Neg.	Neg.	Neg.	0.78	"	"
D.****	"	1030	Neg.	Neg.	Neg.	Neg.	Neg.	0.56	"	" Numerous leucocytes, otherwise negative.

PHENOLSULPHONEPHTHALEIN TEST

A.	10 min. plus 1st hr.	60% excreted.	2nd hr. 15%.	Total 75%.
B.	10 min. plus 1st hr.	50% excreted.	2nd hr. 30%.	Total 80%.
C.	10 min. plus 1st hr.	55% excreted.	2nd hr. 20%.	Total 75%.

NOTE.—These were all comparatively mild cases, and they were used more or less as controls.

*A. Had had large burns of the feet and smaller ones of the hands. His face was erythematous and his eyes showed acute congestion on the more or less chronic conjunctivitis.
**B. Had had severe hand burns, and a very intense conjunctivitis.
***C. Had had a chronic mild conjunctivitis, and an aphonia.
****D. Had no signs of irritation.

BLOOD: These cases showed no blood changes.

GENERAL DISCUSSION OF THE RESULTS

The chemical and microscopic laboratory examinations were carred out as completely as was possible and the negative results were charted as well as the positive pathologic findings. The negative results will serve not only as a guarantee that the specific examinations have been made, but will also furnish a broader basis for further work along this line. Some reactions were found to be negative throughout the series of cases. Fehling's solution failed to reveal any glucose or other reducing substance in these urines. The dilute ferric chloride test never gave the heat labile Burgundy-red reaction of diacetic acid, and on this basis a definite acidosis is ruled out. Of course we can not conclude anything concerning the height of the alkali reserve of the blood from this finding. It may be, and probably is, quite low as we may roughly conclude from the markedly acid urinary reaction and the sediment. Ehrlich's sulphanilic-hydrochloric acid and sodium nitrite reaction for diazo substances was found to be negative in every instance. No melanin reaction was ever noted in the several bromine water oxidizing tests for the pigment. Bile pigments were never found in the urine in quantities sufficient to give the play of colors with fuming nitric acid, and the foam test was always negative.

The daily 24-hour urinary output was at first very low in most cases, and the specific gravity was correspondingly high with the exception of Case I and Case II. In Case I, there was no urine output during the last 24 hours of life, but the anuria was not absolute as there were found 60 c.c. of urine in the bladder at autopsy. However, catheterization nine hours before death had failed to produce a specimen. In Case II, there was intense thirst, and the polydipsia kept the urinary secretion fairly high and the concentration fairly moderate. In all the other cases the forced ingestion of fluids brought the urine output fairly high and reduced the concentration.

The urine in these cases showed uniformly a high acidity. The degree of acidity was in proportion to the severity of the case and was only slightly reduced even with the marked dilution of the urine due to forced ingestion of fluids. The specific gravity varied with the urinary output; it was high at first, but became lower with the dilution of the urine. The amount of albumin present was greatest in the most severe cases and gradually decreased with the scientific management of the cases and disappeared first in the less severe cases and eventually even in the more severe cases. In the mildest cases, Case IX and Case Group X, no albuminuria was ever detected.

The urine urea, both the percentages and the quantitative outputs, and the urine chlorides, percentages and quantitative outputs, were low at first in all fairly severe cases, but under the treatment the output of these substances gradually increased in amount, and, in the milder cases, reached a fairly normal level. These figures serve as a fair index of the impaired renal functional efficiency, especially when considered with the blood urea, and an approximate average of the sodium chloride intake.

The only trace of any pathologic pigment in the urine was the reaction of the urine to dimethylaminobenzaldehyde for urobilinogen in the severe cases,

Cases II and III only. This might be interpreted as indicating a slight temporary functional impairment of the liver.

The microscopic examination of the centrifugated urine sediment substantiates the diagnosis of renal irritation that was made on the basis of the chemical and physical examination of the urine. The quantity of pathologic constituents in the sediment corresponded exactly with the severity of the cases as indicated by other findings. There were hyaline and granular casts, red and white blood cells, renal and bladder epithelial cells, amorphous urates and uric acid crystals in great numbers. At times calcium oxalate crystals, and only occasionally, the sediment of alkaline fermentation, triple phosphates, ammonium urates and calcium carbonates, were found. The sediments all improved markedly and cleared up under the physiologic therapy that was applied.

The blood ureas ranged from 10 mg. per 100 c.c. of blood in the most severe cases to 26 mg. per 100 c.c. of blood in the least severe cases. These findings together with the diminished urea output may be taken as evidence of a renal insufficiency.

The phenolsulphonephthalein excretion tests could not be made until the renal condition had practically cleared up, so far as could be determined by the chemical and microscopic examinations of the urine. The amounts excreted were high, to the extent of even suggesting a hyperpermeability. In only one case (No. III) was there any indication at all of a slow excretion of substances.

Most of the hematologic work on our cases was done between the tenth and fourteenth days after the gassing. There was noted a slight decrease in the number of erythrocytes, this decrease was most marked in the more severe cases. In Case I, the count ran as low as three and one-half million red blood cells with a hemoglobin of 70 per cent, a fairly severe secondary anemia. Even this most severe case on the tenth day after the gassing, nine hours before death, showed a persistent fairly high leucocytosis and no signs of a terminal leucopenia in spite of a definite loss of resistance against the destructive process and the secondary infection. This case showed an apparent decrease in the number of blood platelets which finding differs from that in all the succeeding cases, though the later smears in Case II toward the end also showed fewer platelets, while the earlier smears showed a marked increase in the numbers of these constituents.

Case II, as all the other succeeding cases except the last one, showed a more moderate anemia with the erythrocyte count not falling below four million and the hemoglobin totaling about 75 per cent. The leucocyte counts in Case II were seen to fall from a 29,700 leucocytosis at the tenth day to a 10,800 leucocytosis on the twenty-fifth day, the day on which he died. This was taken as an index of the gradual loss of ground or resistance in the fight. The count remained high enough even at the end, to be considered a mild leucocytosis. The blood platelets were markedly increased at first, but were not so at the end.

Case III, aside from the slight secondary anemia, showed a very gradual drop from a leucocytosis of 25,000 to one of 15,000. This drop, however, was accompanied by a gradual general improvement and a clearing up of the slough-

ing and secondary infection. There is also a definite increase in the number of blood platelets.

Case IV showed the slight secondary anemia and a marked leucocytosis of 25,000 two weeks after having been gassed.

Case V showed also the slight secondary anemia and a leucocytosis of 21,200. The blood platelets were also noted to be increased in numbers.

Case VI showed also a mild secondary anemia and a moderate leucocytosis. The blood platelets were also noticeably increased.

Case VII, the least severe of the series of generally gassed cases, showed no secondary anemia. A fairly high leucocytosis, about 20,000, was found, in spite of the absence of any marked suppuration or generalized secondary infection.

Summarizing the study of the blood in these seven cases of severe mustard gas burns we see that it shows a secondary anemia (reduction of both the number of red blood cells and the hemoglobin), a polymorphonuclear leucocytosis with disturbances in the differential count, such as an increase in the number of bone marrow elements (myelocytes, myeloblasts, bone marrow mononuclears and lymphocytes) and a definite eosinophilia. An excess of young forms of white cells is found. There is also an apparent increase in the number of blood platelets. No evidences of hemolysis were found. A very few red blood cells showing polychromasia and stippling were seen. There was no leucopenia observed in any of these cases, either during the course, or, in the two fatal cases, as an agonal phenomenon. The differential count indicates a disturbance of the bone marrow in the white cell forming group rather than in the red cell forming group. These changes can perhaps be explained by the coincident infection of the skin lesions and the respiratory tract, which all of these cases showed to a greater or less degree. The blood changes ran a fairly parallel course to the severity of the infection. The eosinophilia can be referred to the skin condition, perhaps also to the bronchial.

Under the miscellaneous laboratory examinations we must include the findings in the sputum. In general we may say that the sputum was never blood-tinged but was always more or less mucopurulent in character depending on the severity of the pulmonary affection. In Case III with a bronchopneumonia the sputum was most purulent, frothy and markedly foul in odor, and abundant in amount. On one occasion the patient expectorated a pinkish fibrin-like cast of a bronchus. Smears of this material were found to contain a mixed culture of streptococci and one of the long thick bacillary types of organisms that are found in the mouth. It seemed rational to consider these organisms as the probable etiologic factors in the secondary bronchopneumonia in this case.

The examination of the feces morphologically was negative in most cases, but in Case II at increasing intervals during the last two weeks of his life the patient passed bright red and some slightly changed blood in his involuntary stools. In his last few days the amount of blood passed gradually increased as the patient grew weaker.

Smears of the young furuncles and pus from the old furuncles always

showed a few groups of staphylococci, many degenerating polynuclear leucocytes and much debris.

The temperature charts showed febrile reactions with corresponding pulse and respiration rise, only during the presence and persistence of secondary infection. The high pulse rate in the severer cases would lead one to suspect myocardial injury. This suspicion, however, is not substantiated by the pathologic examination of the heart muscle at autopsy.

Comparing our results with the few reports of research along similar lines found in the literature, the only one of any importance on blood changes due to gassing is that of Miller (*Journal of the Royal Army Medical Corps*, January, 1918, xxx, p. 76). After an extensive amount of work he reported a new blood change in gas poisoning as follows:

1. In cases of gas poisoning in which symptoms persist, there is an increase in the number of lymphocytes relative and absolute in the circulating blood. In slight cases this may not be beyond the normal limits or in excess of what may be met with from other causes. In any marked case, however, the changes are sufficiently striking to be of some importance in cases where the medical officer is in doubt as to the reliance to be placed upon the statements of men complaining of having been gassed.

2. The blood change is elicited by a differential count of the leucocytes, and it may be taken that a count in which the percentage of lymphocytes approaches that of the polymorphonuclear leucocytes indicates that the patient is still suffering from the effects of the gassing, i. e., provided there is no other complicating disease present which might produce a similar change. A slight relative lymphocytosis is not an uncommon finding in men from overseas, or in anyone, so that no great reliance can be placed upon the signs unless the percentage of lymphocytes approaches closely that of the polymorphonuclear cells.

3. The cell which is increased is the ordinary small lymphocyte of the blood. There may be in some cases a diminution in the number of polymorphonuclear leucocytes which will of course accentuate the sign, but the increase of lymphocytes is an absolute one. Morever, it appears in cases with a high leucocyte count.

4. The change is one which develops early, probably within a month of the gassing and continues for a long time; in cases with persistent symptoms for at least eighteen months.

5. The change appears to be independent of the kind of gas and it is shown by patients exhibiting many varieties of symptoms.

Our findings are not in accord with the above conclusions for all gases, and our cases may not be comparable with his. It seems to us to be questionable whether Miller studied and included the blood findings in cases of mustard gas poisoning. He mentions only the two groups of drift gases and shell gases, and does not differentiate the subclasses chemically at all. His last article published early this year came late enough to have the blood changes produced by mustard gas included, yet no mention is made of it and on the basis of the symptoms described we can not conclude that dichlorethylsulphide cases were studied in this series. We discuss this paper because Miller claims that his

sign is present in all chronic gassed cases regardless of the kind of gas to which they had been exposed and independent of the symptomatology presented. Then, too, the pathologic conditions which he favors as the most probable etiologic factor in the production of the lymphocytosis, that is the chronic inflammatory change in the respiratory tract and in the gastric mucosa could very well be present in chronic mustard gas cases. We do not think that such conclusions can be drawn for all types of gassing as yet, but the decision must rest with the results obtained from further studies of cases in which the chemical nature of the gas is known.

Moreover, our findings do not agree at all with those of Pissarello; but it is possible that his negative findings in the urine were due to the mild character of his cases, corresponding to those in our Case Group X.

Mandel and Gibson's observation on the frequency of albuminuria in cases of mustard gas poisoning is confirmed by our work.

CONCLUSIONS

1. Mild cases of mustard gas burns of the skin show no changes in the blood or urine.

2. Moderately severe and severe cases of mustard gas burns of the skin with some involvement of the upper respiratory tract show after the first week definite changes in urine, blood urea and blood.

3. The urinary changes consist in a diminution of the urinary output, increased concentration and acidity, albuminuria, and diminished urea and chloride output. In the sediment there may be found casts, renal epithelium, red blood cells and an increased number of leucocytes. Under forced fluids prompt improvement occurs.

4. Coincident with these urinary changes the blood urea is found to be high, but approaches normal with the improvement in the urinary condition when fluids are forced.

5. The blood shows a slight secondary anemia with a well-marked polymorphonuclear leucocytosis, a definite eosinophilia, and the appearance of myelocytes and young forms of leucocytes. The blood platelets were usually increased. No evidence of hemolysis was found. These changes indicate a disturbance in the white cell formation rather than in the red blood cell group. No leucopenia was noted at any time. The leucocytosis reached its height coincidently with the height of the secondary infection and fell with the improvement of the infection.

6. The temperature, pulse and respiration charts show in the severe cases an initial period of shock. With the development of the necrosis and the secondary infection there is a corresponding febrile reaction.

7. The bacteriologic examination of the infected skin lesions and furuncles showed constantly the presence of staphylococcus pyogenes aureus. In the one bronchial cast obtained streptococci were present.

8. We believe that the changes in the blood and urine may be interpreted as dependent upon the secondary infection and, in part, possibly, to the absorption of toxic products from the necrotic skin, rather than to any direct toxic action of mustard gas.

My thanks are due to Doctor A. S. Warthin for directing this work, to Captain L. L. Roos for the privilege of studying the cases under his care and to Doctor C. V. Weller for many helpful suggestions.

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DIAGNOSIS PER EXCLUSIONEM IN ORDINE: GENERAL AND PSYCHIATRIC REMARKS*

By E. E. Southard, M.D., Boston, Mass.

IS there any excuse for a communication on the general theory of clinical diagnosis? Should not one in the present concrete state of medicine apologize for any generalization or theoretical handling of a topic which has long since passed into the realm of the dead? If medical schools rarely nowadays, and only as a *curiosum*, deal with the sometime familiar disciplines of so-called medical propedeutics and the logic of medicine, is it not for the very good reason that medicine no longer requires any propedeutics or any special overhauling of its logic?

I have two possibly tenuous excuses for the attempted resurrection, namely, first, that it is a canon of mental hygiene to get in imagination as far away as possible from our terrible environment; and secondly, that the realm of dead notions somewhat well befits a pathologist who has gone into psychiatry.

Speaking to a group of eminent clinicians, I need not insist that I myself make no claims to being a diagnostician of the first water. But just as more or less valuable books on elocution are written by persons without color or pretence of oratory, so perhaps one who is not an especially good diagnostician may descant humbly on the matter. Some five years ago, when I became director of the newly founded Psychopathic Hospital in Boston, it became for the first time my duty to deal concretely with a large series of clinical diagnoses. To be sure, before that time, and in fact, in the year 1909, I had been charged with the task of supervising the clinical and pathologic research work of the state institutions for the insane of Massachusetts, and had already at that time begun to agitate upon the manifest errors in diagnosis which appeared in a small but definite minority of cases of mental disease in these institutions, as tested by the stern criteria of the autopsy table. I took an especial interest in errors of diagnosis in that mental disease entity, about which we know the most, namely, general paresis,[1] and found that one of the most active and thoroughly educated state hospital staffs in the country, namely, that of the Danvers State Hospital,[2] was none the less able to make an error of anywhere from 5 to 15 per cent, according to the fineness of the criteria adopted in the disease general paresis. After all, this work and sundry other articles by my associates and myself[3,4,5,6] remained quite upon the theoretical or unapplied level.

Suddenly, in 1912, I was translated to a region in which exceedingly rapid, not to say provisional, or not to say "snap" diagnoses had to be rendered in what almost any one would concede was the most difficult field of clinical diagnosis, namely, the diagnosis of mental disease. When it is remembered that the task at the Psychopathic Hospital is largely the temporary care of acute, incipient, and curable cases together with a consideration of all the most du-

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bious cases in the community,[7] it will be seen that the problem of a reasonably accurate diagnosis in these cases is not at all easy. It is necessary to remember, also, that our task is not that of the alienist so much as that of the psychiatrist, employing these terms in the differential sense recently advocated in a paper on the nomenclature of mental hygiene.[8] It is not the task of the Psychopathic Hospital to determine, except in a minority of cases, the committability or survivability of its patients. Of the first 5000 discharges from the Psychopathic Hospital, over 1700 were discharged as "not insane," a term which signifies, not that the patients had recovered, but that they were regarded as not having been insane during their stay at the hospital (the recoveries are over and above the 1700 "not insane"). In short, the task here is one of securing a basis for treatment and counsel for cases that lie often entirely without the purview of governmental control as mechanized by the probate courts. A large part of our problem is medical in the strict sense and not medicolegal.

I may be pardoned for insisting upon this peculiar and almost unique feature of the Psychopathic Hospital work in Boston, because not even my colleagues in the specialty of mental diseases have readily grasped the point. *Alienists* are a type of physician specializing in medicolegal practice, and their task is to determine alienation; that is, the theoretical or practical committability of their cases in the interest of the public welfare. *Psychiatrists* are a type of physician specializing in mental diseases on a much broader basis, namely, the basis of finer diagnoses, involving groups of mental disease and defect, and the psychopathic trends which fall short of defined psychoses and even the quicksand topics of eccentricity, crankiness, and oddity. *Alienistics*,—a medicolegal field,—is pretty sharply distinguished from practical psychiatry,—a medical field. A good psychiatrist ought to be able to accommodate himself to governmental groups well enough to be a good alienist; but, on the other hand, many a good alienist who has dealt for years with the category of committability only, is unable quite to see the point of a diagnosis of "Psychotic, not insane," or of "Psychopathic, not insane." The question of nomenclature is subordinate; but aside from the question of nomenclature, if the practitioner can not grasp the distinction between insanity in the medicolegal sense and mental disease in the medical sense, he is a man unable to keep pace with the modern progress in psychiatry.

What, we may ask, has the question of psychopathic hospital diagnosis of psychoses that fall short of insanity to do with the topic assigned for this communication? How does this work fit into a discussion of the general theory of clinical diagnosis? Psychiatrists have always taken a good deal of interest in classification. I will remind you only of the eminent instance of Pinel, who in 1809, published a *nosographia methodica*, which is one of the best-known of the old nosologies, a very good general view of which is given in Hosack's publication in 1819.[9] I am afraid, however, that most modern practitioners, and especially in America, would be apt to deride it as out of date, if not fundamentally beside the point of these adventures in classification. Of course these scoffers have the entire interest of science against them in their scoffing. But the modern practical fellow, especially the pragmatic American, little recks such a

small matter as consistency with the general history of science. Nor will I attempt to defend the various excesses of nomenclature to which my psychiatric superiors, both in point of time and in point of capacity, have sometimes perpetrated. It is another queer way which Americans (and I suspect other moderns) have, namely, to confuse the topic of nomenclature with the topic of classification. Classifying for these persons means assigning a name. To be sure, a slight re-reading of that apostle of clarity, John Stuart Mill, would perhaps set these confused minds aright. Still I suppose it is too much to ask of them to re-read even a few chapters of Mill's *System of Logic*.

What, after all, constitutes diagnosis? I do not know whether the Harvard Medical School curriculum is less logical than those of other medical schools that the American Medical Association terms *Class A*, but it is very hard to get from a Harvard Medical School student at any stage, even immediately after securing his M.D., an adequate definition of the terms *diagnosis*, *symptom*, and the like. Yet would any one of us suppose that these terms can be safely dispensed with in practice or in theory? And even if you could somehow show that a pragmatic view of medicine might throw overboard altogether the distinction between disease entity and disease symptom, nevertheless the books are full of these terms used in a variety of ways, and I am sure it ought to be the duty of every medical course to offer some pabulum (whether propedeutic or by way of appendix) on these matters, which were doubtless comprised in the forgotten and discounted field of so-called Medical Logic.

Many a favorite textbook in the practice of medicine fails to make any point whatever of this distinction, and plumps one forthwith into a discussion,—e. g., of typhoid fever,—jauntily assuming that the student somehow knows by intuition the meanings of the terms, *definition*, *entity*, *diagnosis*, *symptom*, *symptom-complex*, *syndrome*, and the like. Perhaps, however, it is better to leave out general remarks in this direction than to put in some which are found in certain other textbooks that have run into many editions. Strümpell[10] makes no special point of the matter but insists in a preliminary note upon the importance of diagnosis, of clinical observation, and of keeping the common courses of all diseases in mind. Here, perhaps, is the most commonplace remark nowadays about diagnosis: diagnosis, namely, is constituted by observation, according to these authors. In fact, there is one textbook (Wilson[11]) that summarily states upon its title page, that the whole art of medicine is in observation. On a later page, it is insisted not quite so broadly, that "It is certainly true that the art of diagnosis is an art of observation;" and again, "The facts of pathology and semiology and the natural history of the diseases constitute the basis of diagnosis." This latter statement seems almost equivalent to the statement that the facts of disease are the basis of diagnosis, which may be in one sense true, but is so little helpful that it might well be left unsaid. Another recent author (Hall[12]) states that "The art of diagnosis consists, then, in gathering all accessible data and arriving at that conclusion which seems the most reasonable as the probable cause of the trouble." This definition evidently goes beyond the former, namely, "Diagnosis is constituted by observation," by considering that the reason is necessary over and above observation. Put in these terms, of course no one of us would care to say that diagnosis consists in gathering

data. Put baldly, it is certainly untrue to say that the collecting of facts constitutes the art of distinguishing amongst these facts. Yet the whole trend of recent work runs in the direction of insisting upon observation at the expense of reason. And, whether or no we teachers are entirely clear in our own minds as to the distinction between diagnosis and the mere recognition of fact as such, certainly our students are not always clear. A student will give the "diagnosis" *fever* or *rose spot*, when he would scoff at making the "diagnosis," *It is raining*, or *The engine is skipping*. If this be diagnosis, make the most of it! Of course, diagnosis is clearly a form of recognition, a form of knowledge, but there seems to be no warrant in raising every elementary form of awareness, kenning, or recognition to the level of diagnosis, which term bears within itself a manifest prefix, suggesting distinction, differentiation, sundering. All my own medical teachers, and I do not doubt the majority of those of my listeners, insisted upon the value of accurate observation. Few of them insisted upon the importance of correct reasoning. Most of them, I take it, partly as a matter of self-defense as they were growing older, were quite sure that maturity of judgment was a thing not readily attained. It never seemed to occur to these teachers that, as the powers of observation were on the wane, the powers of right judgment were to increase. In brief, these teachers, without ever once using the term *logic*, and hardly ever the term *reason*, managed to get into their homilies for students the idea that there was something besides observation, namely, what they called common sense or knowledge of fundamentals, or keeping essential cases in mind, or ripeness of clinical experience, and the like.

Though I believe some course in propedeutics might well be constructed to contain the main principles of the logic of medicine, yet that is not the point of the present argument. Basing my notion upon the practical experience of the last few years, in which I have had contact with clinical diagnosis, always with the autopsy criterion more or less consciously in mind, I want to argue for a more extensive application of the principle of logic in practical diagnosis, and especially the practical diagnosis of the tyro. Perhaps you will think my argument is nothing more or less than a rehabilitation of the diagnosis by exclusion of the older authors. To some extent, the argument does follow that line, though the arguments have been derived from recent practical experience in off-hand and professional diagnosis, and from certain logical considerations. That older argument is found very well expressed in DaCosta's book so long ago as 1864.[13] DaCosta's book, according to an enthusiastic Philadelphian (Wilson[11]) marked an epoch in the progress of internal medicine; and surely many of DaCosta's distinctions are found in several textbooks built upon the lines of his book for many decades after 1864. DaCosta distinguished direct and indirect diagnosis. Indirect diagnosis by exclusion, according to DaCosta "is not on ordinary occasions much employed *nor indeed is it to be recommended*" (italics mine). It is this dictum of DaCosta which I would think ought to be combated in any summing up of present-day processes in diagnosis.

The reasons why DaCosta felt that diagnosis by exclusion was not to be recommended were assigned by him as follows: First, "to prove what a thing is by proving all that it is not, is a very tedious process." Secondly, DaCosta went on to say, "it is difficult to think of all the possibilities." And thirdly, he

said, "pathology is in an imperfect state." Now, as for the latter two reasons, it is clear that the process of direct diagnosis is equally subject to the pitfalls of imperfect pathology, and equally subject to the charge that it is hard to think of all the possibilities. I myself can only believe that these two latter so-called drawbacks are not drawbacks worse for diagnosis by exclusion than for any other form of diagnosis. Accordingly, I believe that DaCosta's objection to diagnosis by exclusion reduces its tediousness; but should we hesitate to say to our students that it is better to be tedious than wrong? The technic of DaCosta's process may be elicited in his own words:

"To cite a case in illustration. A person consults us for a cough brought on by exposure. He has been sick for four or five days, having been previously in good health. We notice, on examining him, that his breathing is hurried, and that he has fever; the lower portion of one side of the chest is dull on percussion, and the respiration there is wanting; the action and sounds of the heart are normal. The facts point to the lung or its covering as the seat of the disorder. We know, furthermore, from the history and the febrile symptoms, that we have to deal with an acute affection. What are the acute pulmonary affections? Acute bronchitis; acute phthisis; acute pleurisy; acute pneumonia. In all there is fever, cough, and impaired breathing. Is it acute pneumonia? No; for, notwithstanding there is in this complaint, in addition to the general symptoms mentioned, dullness on percussion, such as we have here, the dullness is associated with a blowing respiration; whereas in the case before us no respiration is heard. Let us look at the sputum, and see if it is tenacious and rusty colored. It is not; it is thin and frothy. Moreover, the breathing, although hurried, is, when counted, found to be less hurried than it is in inflammation of the lungs. But acute pleurisy may explain all the signs. The patient, too, when questioned, states that he had at the onset a sharp pain in his side; and this we are aware takes place in pleurisy. The vocal vibrations, likewise, are noticed to be absent on one side of the chest, which, when carefully measured, is evidently enlarged. This corresponds in all points with what happens in pleurisy in the stage of effusion. The disease *is*, therefore, acute pleurisy in the stage of effusion. We finish the diagnosis by ascertaining the existence or nonexistence of other maladies, and by taking note of the severity of the complaint; that it has occurred in a young and robust person of good habits; and that the symptomatic fever is very active."

But what is a direct diagnosis,—one not made by exclusion? According to Wilson, "A direct diagnosis is made when the history of the case and the clinical phenomena are sufficient to warrant a positive conclusion." Wilson goes on to say that a diagnosis by exclusion differs from differential diagnosis only in scope. Strange as this phrase may sound, it strikes me that there is a good deal of truth concealed in it. I feel that, so far from admitting with DaCosta, that diagnosis by exclusion is not much employed or to be recommended, practically every diagnosis is by exclusion, whether consciously or unconsciously.

Musser remarks concerning diagnosis that "the data collected are sufficient to warrant a positive conclusion. The direct method is scientific, rational, and most practical. It is a practice of purely inductive reasoning." I am not sure whether it would not be sounder to say that it is a process of purely *deductive* reasoning, but modern logicians have conclusively enough proved that practically all reasoning is both inductive and deductive, so that it would not pay to quibble over the claim that direct diagnosis is "a process of purely inductive reasoning." As to the method of diagnosis by exclusion, Musser remarks, "Thus, a symptom group may suggest several diseases; each affection must be passed in review and excluded until one is found which closely corresponds to the data of the case under consideration." In short, it would seem that diagnosis by

exclusion is an effect of the *force majeure* of complex and obscure data. The battle is easily won when it is a question of perceiving a symptom and suspecting a disease, whereupon all "the data collected are sufficient to warrant a positive conclusion."

Now, possibly it is the complex and obscure nature of mental disease which has caused me to feel that diagnosis by exclusion is a method that requires rehabilitation in the minds of teachers and in the pages of textbooks. In medicine and biology at large in the middle of the nineteenth century, it was the fashion to denounce speculation and extol observation. So many of the medical and biological sciences depended upon the microscope and the visual process, that nothing was more natural than to see great virtue in observation as compared with the vagaries of the *Naturphilosophie*.[15] We are now so far beyond the range of that old *Naturphilosophie* (unless the idea of Pan-Germanism may be regarded as a remote result thereof), that it should be quite safe to uphold the reason as entitled to a seat beside observation in the process of diagnosis. Applied logic accords to observation its full worth. Secondly, a proper value is assigned to what may be inaccurately summed up in the phrase *comparative method*. It is the comparative method probably that is being used in diagnosis for the most part at the present day. That is, one picks a symptom, suspects a disease, constructs a supposititious diagnosis, and proceeds to compare it with all the data of memory or reference books. It is all one, whether you pick one symptom—e. g., the so-called presenting symptom[15] popularized by Richard Cabot,—or assemble a symptom group; the process remains the same, that of matching the data of the case with some supposititious diagnosis. Now in the field of mental disease probably every one of you has had the experience of matching virtually all the symptoms of a case with the majority of those given in the textbooks for several different mental diseases. In short, the comparative or matching process has been only too successful, and the diagnosis might well be rendered by lot from amongst a not very small group of textbook headings.

Of course, the comparative method involves the use of observation also. The distinction between observational recognition of a condition and the comparative determination of a disease by a direct method, is not a mutually exclusive distinction. So also in respect to the third method of applied logic, namely, the statistical method. The statistical method requires both observation and comparison, but entails also certain new features. Probably Richard Cabot has popularized the statistical method of diagnosis more than any other recent author. Cabot finds a presenting symptom which becomes to him a lead. This presenting symptom is often something complained of by the patient, but also is often something noted by the physician that the patient did not subjectively recognize. Cabot has founded a differential diagnosis upon a selection of the most common presenting symptoms. He goes on to list the causes of these symptoms by their frequency, and then, to use his picturesque phrase, "follows the symptom home." Following the symptom home means, naturally, employing all manner of comparative and observational methods in addition to the merely statistical one. Nor do I wish to give the impression that Cabot overemphasizes the statistical method in his account. He merely emphasizes it more than most previous authors. Nor would his account fail to insist that observation is indis-

pensable, for he carefully states that diagnoses are missed usually because physical signs are not recognized. That is, for Cabot, poor diagnosis is usually a matter of poor observation. But occasionally diagnoses are poor on account of poor reasoning, and Cabot's book is an argument for a more comprehensive grasp of the possibilities of diagnosis. Others may insist upon the recognition of the symptoms and signs by proper methods of observation, and Cabot, like many others, has in other works given an account of these matters along approved lines; but he dreams for the purpose of differential diagnosis of a "cash-register of causes." He wants possibilities sifted. He wants clues, radiations, and leadings followed out along lines that are essentially statistical. One proceeds from the presenting symptom to the possible causes; from the possible causes to the probable causes, and from the probable causes to the actual cause. In the technic of this determination, Cabot, as is well known, much insists upon the statistical configuration of the different conditions in which the various presenting symptoms are found.

Cabot notes that physicians in the matter of differential diagnosis "are very suspicious of any attempt to tabulate their methods of reasoning." He speaks of profiting much by Herbert French's *Index of Diagnosis*[16] (first published in 1912), a book which I find is greatly affected by medical students of my own acquaintance. French claims his index to be an index of main symptoms, though there seems to be no internal evidence in the book just how these main symptoms were selected. French, like Cabot, deals largely though not exclusively with symptoms complained of.

It is readily seen that Cabot's ideas (though they would have been readily comprehended by DaCosta in 1864, since they are founded upon the statistical principle which had already been a few decades in vogue in DaCosta's time) would not have appealed especially to him as important in the process of direct diagnosis. Feeling as DaCosta did concerning diagnosis by exclusion as a *dernier ressort*, he would not have seen the compelling value of Cabot's statistical frequency tables for the distribution of symptoms in different conditions. Moreover, it is doubtful whether in 1864 hospital records were so extensively kept as nowadays, despite the fact that intensive records of special cases may have been kept at a relatively higher standard than now prevails in institutions where the real work is done more by interns than by visiting physicians.

The situation, then, is that in some cases what might be called an observational diagnosis can be rendered. Personally, I should feel that the term *diagnosis* was being prostituted somewhat when the diseased condition is recognized forthwith on the basis of some pathognomonic symptom or combination of symptoms. But let the phrase pass; the result of naming the disease and getting a practical basis for treatment is attained by a process of pure observation. The so-called direct method of diagnosis is hardly on a higher plane logically speaking than that of observation in many cases; but in others, and perhaps in the majority of cases, this process of differential diagnosis by the so-called direct method, is one of comparison; that is, of matching the phenomena of the disease observed with those of some classical or textbook type. The unduly maligned method of indirect diagnosis, or diagnosis by exclusion, likewise employs comparison inasmuch as it excludes disease after disease by discovering that not

enough exists to match the types in question. Having risen, accordingly, from a process of direct recognition (*gnosis* rather than *diagnosis* in any logical sense) to a process of somewhat less direct differential diagnosis by a positive matching or a negative excluding process, we finally arrive at a more modern technic of studying the frequency of symptoms in certain large groups of comparatively well observed cases (the majority of Cabot's tables deal with 250 cases analysed at the Massachusetts General Hospital). We notice that the process of observation is indispensable throughout. Extreme exactitude of observation is not perhaps so necessary in statistics as in individual cases; at least errors of observation may be assumed to balance themselves to some degree.

Is there no further sharpening of our technic of diagnosis? In the practical handling of the diagnostic problem at the Psychopathic Hospital, in the course of two years' observation I became interested in the fact that, where diagnoses were not matters of mere observation and direct differentiation, but where processes of exclusion were necessary, I found myself endeavoring to exclude conditions in a certain *definite order*. It is this ordinal principle which I believe might constitute an advance in practical diagnosis, were it to be insisted upon in still other branches of medicine than psychiatry. I have recently made some endeavor to apply the principle to the situation in clinical neurology but shall not here mention the results of that inquiry in any detail. After the first two years of off-hand and provisional diagnoses at the Psychopathic Hospital, I then considered the matter of exclusion in a definite order for some three years before laying down the order in question (see below). I think it would be presumptuous for any one in any special branch of medicine to draw up a definite order of diagnoses in any other. For example, however convinced I might be that diagnoses in dermatology are actually made consciously or unconsciously by some process of successive exclusion of conditions in a definite order, I should not (as I am far from being a dermatologist) have the slightest ground for suggesting an order for dermatological diagnoses, or a list of conditions to be put in order. Not being an internist in the field of cardiac disease (that is to say, not being in any sense an expert with the electrocardiograph and all the rest), I certainly could not advocate any particular order of diagnosis for heart disease, however strongly I might be convinced that such an order must exist.

At this point, I looked into certain works on logic to learn what might be said concerning these different principles of diagnosis, and found in the late Josiah Royce's contribution entitled "The Principle of Order" in the *Encyclopedia on Philosophical Sciences,* an exposition very much to the point.[17]

I presume that most of us have few memories of logic except the syllogistic logic of such college textbooks as that of Jevons. Some of the older amongst us will still have used Mill's *System of Logic,* or textbooks closely modeled thereupon. The more recent advances in applied logic are a closed book to most college and medical students, but in addition to so-called formal logic used as an irregular discipline in most colleges, there is an applied logic or methodology which deals with the norms of thought as applied to the methods of the special sciences. The formal logic of a book like that of Jevons is only a very subordinate part of logic as at present defined. Royce speaks of the new doctrine as

the science of order. This science, he says, is today in a very progressive condition, is in some notable respects new, and offers inexhaustible opportunities for future progress. Already in the Socratic and Platonic handling of these topics, the systematic nature of the world's construction, the objectivity of the world permitting inference concerning its various truths and the order that rational processes show, had already become clear. Types, forms, and relations are at least as real as the facts of the physical world. Aristotle, Bacon, and still more importantly, Galileo, made important advances in logic. Today no one will question that every science in dealing with its facts must employ methods of classification, in no wise different from the method used by Socrates in his dialects. To be sure, a science which uses only methods of classification must now be regarded as a very young science. Botany and zoology have long since passed the phase in which classification is the dominant interest. Anthropology, on the other hand, is largely classifying still, though there is some tendency to the development of a higher method of logic, the comparative study of the forms and results of human culture.

Royce mentions that, amongst the medical sciences, psychiatry is just now emerging from a stage in which the bulk of the science was made up of the classification of cases, symptoms, and disorders. Psychiatry is now about to work on a higher plane of methods. The more complex the facts, the harder it is for a science to get beyond this first stage of classification.

What are these higher processes of applied logic? There are mainly two: The method of comparison, and the statistical method. The comparative method compares the corresponding stages in the various processes of products of natural evolution in the science in question; whereas the statistical method uses exact enumerations as the basis of its science. Of course, the two methods are not always sharply to be distinguished; whenever one has to compare numerous evolutionary processes, all the results of these processes have to be enumerated. In these instances, however, the statistical method is merely an auxiliary to the comparative method. When, however, we come to such matters as the mortality tables of insurance, the sociology of marriage and divorce, of suicide and crime, or of commerce and industry, we are dealing with topics in which the statistical method is virtually the only one at present available. We study, for instance, how human mortality varies with age; how the science of an organ or an organism follows conditions determined by heredity or environment. As a result of such statistical processes, the statistician becomes able to deal with aggregations or blocks of facts; orders or aggregations which may be treated as units of a higher order.

When sciences become developed still further, these two methods of comparison and statistics are used in a still more intimate manner, combined in a method which Royce terms the *organized combination of theory and experience.* By means of the statistical and comparative method, we discover laws of nature that have a certain degree of probability, the degrees of which we may trust on the basis of fair samples of the phenomena of the given science. We then construct laws on the basis of hypotheses derived directly from fair samples of fact. Hypotheses thus drawn may be of the simple type directly

refutable or directly verifiable by immediate recourse to the facts; or on the other hand, hypotheses may require much more work for their testing. In fact, the more direct the proof, the more valuable the hypothesis, since the success of the hypothesis would here depend upon the falling-in-line of vast numbers of facts which on no other basis could be supposed to fall in line. To combine hypothesis, theory, and observation, we first draw up a hypothesis regarding the constitution or laws of some region of physical fact. Upon the basis of this hypothesis, we make an extensive and exact deductive theory as to what *ought* to be present if the hypothesis is true. "The more extensive, exact, and systematic the theory thus made possible proves to be, the larger are the possible samples of the consequences of the hypothesis which are available." We then collect samples of facts by means of observation and experiment, and proceed to compare them with results of our elaborate deductive theory. The more elaborate and extensive our theory, the larger the range of facts that we can draw upon for comparison. We are not now restricted to noting what proportion of members of a sample have certain characters. On the other hand, if the deductive theory is a highly developed and elaborate one, we shall find that almost any sample available for comparison is minutely verifiable in detail with some part of the original hypothesis. In short, the value of this method depends upon "the exactness, the order, and the systematic character of the concepts in terms of which the hypotheses thus directly tested are defined." It would thus appear from this highly condensed statement of Royce's view, that "the organized union of theory with observation requires for its perfection concepts and systems of concepts which permit of precise and extended deductive reasonings." It is surprising how small the samples need to be when it comes to a judgment as to the applicability of a highly complex hypothesis. A few small samples taken from widely separated parts of the system will prove or disprove the virtues of the hypothesis.

Without asserting that medicine is yet in a stage to profit like physics and chemistry from this organized combination of hypothesis, theory, and observation, it is clear that many parts of medicine are far beyond the application of mere statistics or of mere comparison, and still farther beyond the modest virtues of pure observation.

Without venturing further at this time into methodology and modern applied logic, it is clear that mere observation, mere comparison of stages, mere enumeration, are not the whole story in any science. If the medical sciences are going to advance in their logic, it is more than likely that their logical advance will take place in the direction of a greater insistence upon order. I hold accordingly that, if Royce's exposition of certain modern developments in logic is a sound one, the next stage of development in medical thinking will be a reduction of its interests more and more to order and system. There is reason to hope that by the reduction of medical as well as any other scientific facts to order systems, a greater and greater success in deduction will be attained. I conclude, therefore, that when I found our process of diagnosis at the Psychopathic Hospital employing more and more the concept of order, I was simply discovering a small fact bobbing in the big stream of logical advance.

In the light of present knowledge, how almost naïve and childish appears the old dictum that disease is life under altered conditions! Here were but two elements: life on the one hand, and change on the other. Each contains a host of undiscovered statements of fact. How slender a contribution appears the claim that diseases must be instances of either the augmentation, the diminution, or the mere modification without increase or decrease of structures or functions. To be sure, bacteriology shortly yielded a dyadic system of germ on the one hand and host on the other, which for the moment and for a decade or so allowed one to hope that the formula "Disease is life under altered conditions" might be simply rendered into, "Disease is the effect upon an organism of a germ." Then came the contentions of Metchnikoff concerning phagocytosis, and the more complex interrelations of the host with its contained germ.

Shortly, in the nineties arrived triadic conceptions of the interrelation of the organism, the foreign substance, and sundry intermediary bodies; and early in this century was unfolded the still more mysterious situation of anaphylaxis. In short, the problems of medicine are becoming more and more rich and complex, more and more verifiable by small samples of fact taken at widely diverse parts of the system.

The rapid complication of the research situation in medicine at large, as typified especially by the facts of immunology, has its reflection also in the slower moving departments of clinical diagnosis. We see in textbook after textbook insistence on diagnosis as a matter of observation (going back very far, for example, to Baglivi[18]). We then found, as in virtually all the medical textbooks in the latter half of the nineteenth century, a new form of assurance: The diagnostician is not now satisfied with what he calls direct diagnosis.

The aim here is to enroll the case in some definite group of diseases recognized by pathology. The difference between perceiving that "this fruit is an orange" and scientific recognition of a diagnosis is merely a question of degree. It is not so easy to say that "this is a case of typhoid fever," as it is to say that this fruit is an orange, because of the more concealed and special nature of the points on which we rest our diagnosis of typhoid fever. The method is one of comparison of certain perceived characters or features with certain signs already known to us as pertaining to certain disease groups. Whether the symptoms are simple, like a friction rub, or complex, like the chemical analysis of a secretion; whether the symptoms are present at the time of examination or are merely anamnestic, from the diagnostic point of view, they are speedily divided into pathognomonic symptoms on the one hand, and more general ones on the other. The tubercle bacillus or the Argyll-Robertson pupil might be mentioned as examples of pathognomonic symptoms in this broad sense; whereas fever and vomiting would be examples of symptoms which belong in a great number of disease groups. But whatever the kinds of symptoms we recognize, the process of diagnosis appears to be one of comparison of those symptoms that we perceive with such symptoms as we know to characterize a given group of diseases, and upon the discovery that the symptoms of the disease in hand correspond with the symptoms of the disease type

which we know from the books or from experience. We draw a conclusion, then, on the basis of similarity of symptoms. We may draw this conclusion from a pathognomonic symptom, which beyond any question indicates the existence of a given disease; or if no pathognomonic symptoms are present, we may ground our diagnosis upon the harmony between the general symptoms in our patient and the symptoms that belong to some described disease; and of course we are throughout well aware how unsuccessful may be a diagnosis based largely on the similarity of general symptoms to those of the books. This method of diagnosis, which we may briefly term the "type-matching" method, is doubtless the one extolled by the older workers under the name direct diagnosis. It represents an advance upon purely observational diagnosis,—that is, diagnosis by inspection,—and is a form of diagnosis by comparison.

Diagnosis by exclusion or by differentiation is a method somewhat decried by older workers and now brought into great prominence by such work as that of Cabot and of Herbert French. Though there is nothing logically new in this work, there is a new emphasis in it. It is still, logically speaking, an application of the comparative method greatly bolstered, as Cabot handles it, by the statistical method.

The general nature of differential diagnosis is somewhat as follows: As it is imposible to consider all the phenomena in a given disease, we first select a group of diseases in which a certain sign is found. We look in the case under observation for some more or less outstanding symptom. This common symptom which we would use as the point of comparison amongst diseases, is called by Bieganski the *index of differentiation* or the difference indicator. Cabot has more recently termed one form of it the presenting symptom. This indicator or presenting symptom is chosen because we by experience know that it occurs in a large number of diseases. To be sure, it is much better not to take a too-general indicator. Thus, in the question of typhoid fever, it would not be so advantageous to begin with fever, perhaps, as to begin with diarrhea. The process of differentiation now begins: We compare the case under observation with those diseases which we have found to be somewhat similar thereto. We pass from one disease group to another. We constantly keep upon one side the observed case with all its symptoms, and on the other the total series of diseases which in a certain respect are similar to it, namely, in respect of the common trait, index of differentiation, or presenting symptom. We proceed to look for differences. The observed case may not belong in a group because it does not possess the symptom which is constant in that group; though the indicator is possessed by both diseases, a symptom constantly present in the compared type is absent in the observed case.

Or the observed case may not belong in the compared group because there is a symptom in the observed case which never occurs in the compared group.

Again, the observed case is not the disease with which we are comparing it because we know that in the compared disease a symptom constantly occurs which is the direct opposite of some symptom observed in the case in hand.

Moreover, there may be an incongruence of symptoms of a quantitative or qualitative nature, a difference which does not proceed to the point of complete absence or perfect antagonism of symptoms.

Following is a table which embodies the process-types of clinical diagnosis now in vogue:

TABLE OF PROCESS TYPES OF DIAGNOSIS

I. Inspection.
II. Expectation.
III. Induction.
IV. Comparison
  (a) Similarity.
  (b) Similarity and difference.
  (c) Difference.
V. Ex juvantibus.
VI. Ex nocentibus.

I may say at the outset that it is the endeavor of this paper, granting each of the three subordinate methods under the head of Comparison to be a separate logical method of diagnosis, to add a ninth method. This ninth method I shall choose to call "*Diagnosis per Exclusionem in Ordine.*" *Diagnosis per exclusionem in ordine* is merely a method of employing logical comparison of Type IV (c) of the above table *in an orderly manner.*

But before attempting to speak of this newly described type of diagnosis I must briefly describe the eight classical methods so that I may, if possible, demonstrate that the ninth or proposed new method has novelty. For the purposes of this discussion I have gone rapidly over a great many of the older textbooks of medicine, studying largely the logical remarks by their authors in the prefaces and introductions thereto. I then examined many of the textbooks in Medical Logic which were for some years the vogue in medical schools. From the study of textbooks, largely in the latter half of the nineteenth century, and from the study of works on Medical Logic I have arranged and combined the methods of the above table. I have been especially aided by the modern work of Bieganski, a Polish work available to me in German translation from its second edition. This work may be referred to for a good summary of the older points of view, together with the fruits of some Polish polemic in which Bieganski had for some years been engaged. The older work of Oesterlen,[20] published in Tübingen in 1852 and translated into English[21] in the Sydenham Series in 1855, is almost barren for modern purposes (so much so that I found the leaves uncut both of the original and of the translation in the New York Academy of Medicine!) Of still older literature, the Medical Logic of Sir Gilbert Blane,[22] illustrated by conclusions concerning yellow fever, is of great interest, though his classification of the elementary principles of life as generative, conservative, temperative, assimilative, formative, restorative, motive, sensitive, appetitive and sympathetic, is an example of categories which, however true and from various points of view feasible they may be, are of little diagnostic value. This older work often fails to distinguish the question of classification from the question of what is to be classified. Sir Gilbert Blane's work upon yellow fever, and especially upon scurvy, derived

from his expert contact with marine diseases in the British West Indian campaigns, is of greater value than his excursions into logic. Blumenbach calls Sir Gilbert Blane the most learned and classical physician of the age, but despite this German appreciation, little has been done in Germany of an original nature on medical logic. Oesterlen appears to be in the general nature of a physician's reaction to the logic of John Stuart Mill. Apparently someone was impressed with the possible value of such work as Oesterlen's, and Francis Ogston was given a new chair in Aberdeen as Professor of Medical Logic and Jurisprudence. In a syllabus[23] of his highly interesting course of thirty-two lectures, he refers to his indebtedness to John Stuart Mill and to Oesterlen, traces the history of the topic from Aristotle to Bacon, thence to Blane and Oesterlen, and comments upon the absurd distrust of theory which he found prevailing in Britain. Ogston called the merest routine practitioner a bold speculator and imperfect observer of facts. He remarks that the limits of pure observation in medicine are soon reached and discusses in separate chapters the inductive or analytic method as opposed to the deductive or synthetic method, rightly holding that the latter is a much more important concern of medicine than the former. Under the inductive or analytic method Ogston considers the processes of observation, comparison and analogy, and the numerical method. Under the deductive or synthetic method he considers first the process of analysis for deductive purposes, then the process of ratiocination and of verification. He discusses, among the processes subsidiary to induction, such matters as simple observation, experiment, hypothesis, analogy, the numerical method, terminology and classification. Ogston denounces the current nosologies as obstructive and inelastic and devotes special attention to what he calls the fallacies of nonobservation as opposed to the fallacies of malobservation. Much of this suspicion of Ogston can be traced in Oesterlen and Sir Gilbert Blane, to say nothing of their masters in logic, John Stuart Mill and Sir Francis Bacon.

Sir Gilbert Blane had, for example, in 1819 spoken of the sources of error in medicine as (*a*) the fallacy and danger of hypothetical and theoretical reasoning as especially demonstrated (according to Blane) in Boerhaave, (*b*) the diversity of constitutions, (*c*) the difficulty of "appreciating the salutary efforts of nature and of discriminating them from the operations of art," (*d*) superstition, (*e*) the ambiguity of language, and (*f*) the fallacy of testimonial.

Much can still be gained, no doubt, from a perusal of such works as those of Sir Gilbert Blane, Oesterlen and Ogston, and still more could doubtless be gained by the physician from a close study of John Stuart Mill and his predecessors in pure logic, but these studies were almost wholly given over with the onset of the evolutionary theory in the late fifties, with the crowding developments of pathology and physiology and especially of the bacteriology of the eighties and the immunology of the nineties of the last century. There has, in fact, crept over us the feeling that logical method is an inheritance of us all in like degree and that whatever we do not know of logic at the outset of medical practice we shall never learn. It is precisely the popular single volume textbooks that fail to yield much of practical value to the medical student seek-

ing to perfect himself in the *logic* of diagnosis. The dictum, especially of Da Costa and of his successors in the manufacture of single volume textbooks, namely, that the art of medicine consists in observation, has apparently abolished the necessity of logic. Carried away by the magic of this word "observation," many authors of physiologic works dealing with the most intricate discussions and fine-drawn conclusions cheerfully called their inductions and deductions by the term "observations." The obvious fact is that diagnosis does not consist in observation at all. Diagnosis requires observation, proceeds upon a basis of observation, but is in itself a process of combination, of reasoning, of calculation, or of some higher kind of intellectual process which takes observation for granted, uses and chooses amongst observations, but in no whit makes them.

Amongst the methods tabulated above I have first set down, following many of the books, *diagnosis by inspection.* Here, at the outset, it may be inquired: "Are we not terming a method of diagnosis what is nothing but a method of observation?" This I freely concede. The names of diseases are achieved by a process of inspection. The result is what we term a diagnosis, but the process by which the so-called diagnosis or disease-name is arrived at is not a process of reasoning at all, but (as stated above) a process akin to the statement, *It is raining,* or *The engine is skipping.* In short, no process of diagnosis in the logical sense is here being used. A diagnosis or disease-name is achieved, but reasoning is not employed. It is only, then, by courtesy that we include inspection under the process-types. The diagnosis follows the inspection as night follows day, or as black follows white, or as man follows woman. The process is one of association of a perfectly simple type. This kind of so-called diagnosis can be made by laymen often as well as by physicians. I am afraid that the ideals of many medical teachers, as they are got by the eager students, consist in teaching them thumb rules of inspection rather than the more tedious and complicated methods of diagnosis. I recalled above how Da Costa spoke of diagnosis by exclusion as a tedious method.

The second method tabulated above is one that I have presumed to term the method of *diagnosis by expectation.* We are familiar with the so-called expectant treatment in therapeutics, but, so far as I know, attention has not been called to the method of diagnosis by expectation. This is, of course, particularly employed in the fulminating, acute diseases on one hand and the chronic diseases on the other. In the one instance there may not be facts enough to permit a diagnosis by inspection and there may not be time enough to permit elaborate comparisons; accordingly, diagnosis goes by the board until an autopsy either is or is not made. As for the slow, hesitating course of certain diseases, the Micawber attitude is still easier to assume.

I suspect that the method *by induction* is commonly employed in a manner not far removed from the process of expectation. This method by induction, unlike the method by expectation, is mentioned in the classical works, and also in the modern work of Bieganski. One concludes that the patient looks tuberculous. Here is the suggestion of a diagnosis by inspection. Perhaps one is an office practitioner and time forbids exactitude. One examines the pulmonary

apex and discovers suspicions of dullness. One requests the sputum and proceeds to a positive diagnosis of tuberculosis on the basis of tubercle bacilli found in the sputum. Here is a successful case of diagnosis by induction by a sort of skipping of intermediaries (to use James's phrase) and by the least possible work. If the diagnosis is successful, well and good! If unsuccessful, one must proceed to more elaborate methods. It is always possible, too, that the patient may have been suffering from a combination of two or more diseases and that the tuberculosis e. g. found may be the lesser of two important conditions. One ought not, and I do not, condemn this method by induction just because it is not time-consuming and just because it does not succeed in all cases. In the hands of the expert the method of diagnosis by induction (as the phrase is here used) and the method of diagnosis by inspection are highly commendable methods. In a pragmatic age one ought not to denounce them. From the standpoint of a medical student, however, it would seem wise not to dazzle him with the brilliancies of inspection and induction (in the above narrow sense), but one ought to expound to him the nature of the more complex methods which he must often use in cases that are themselves at all complex.

The methods of *diagnosis ex juvantibus* and *ex nocentibus* tabulated above are in a sense experimental methods of diagnosis on all fours with the method by induction. The diagnosis of syphilis by the administration of antisyphilitic drugs and the procuring of a cure or an alleviation of symptoms is an example of diagnosis *ex juvantibus.* The provocative Wassermann reaction upon the administration of salvarsan is an example of the method of diagnosis *ex nocentibus.* It would be a mistake to consider the administration of drugs for these purposes therapeutic. The methods are methods of diagnosis purely.

Dismissing the methods of inspection, expectation, induction, *ex juvantibus* and *ex nocentibus,* we come to the methods of *diagnosis by comparison,* to which I hope to point out a small addition or modification which I conceive to be of value. Earlier in my communication I have sufficiently discussed these methods and I pointed out the necessity under which we labor of using the method of diagnosis by exclusion in cases where there are no indicator symptoms or presenting symptoms (to use Cabot's phrase for certain indicator symptoms). I wish to illustrate this method of *diagnosis per exclusionem in ordine* from the field of mental diseases, rehearsing the main groups of a practical key[24] which has been built up on the basis of Psychopathic Hospital data.

In passing, I may say that psychiatrists are far more at one in the matter of diagnosis than the general medical man is apt to believe. The unanimity in point of view is far greater than one would suspect from certain nomenclatural differences. The nomenclature of psychiatry is by no means as fixed at the present writing as the nomenclature of dermatology. Yet the unanimity of psychiatrists concerning the major groups of mental disease is, I make bold to say, almost as great, if not quite as great, as the unanimity of dermatologists concerning their main groups. The specialists in psychiatry have for some years past been much interested in proposals of the American Medico-Psychological Association to secure a thorough and acceptable classification of mental diseases to which the State institutions for the custodial insane could conform. The

classification adopted by the Medico-Psychological Association in 1917 is, in general, a highly acceptable one.[25] Probably no member of the committee charged with making the classification is entirely satisfied with it in details. Some diagnosticians go so far as to say that in the interest of the patient no classification in the sense of the statistical tables of institutions is worth while, since every instance of mental disease is virtually *sui generis*. There is, of course, much truth in this contention, and the good therapeutist never forgets this fact, borne in upon the mind as it is by the tremendous individual variety of the psychogenic reactions of the individual as such. I found that most of the leading American textbooks of psychiatry were also practically at one in the major categories, despite perturbing difficulties in terminology.

The task of the Psychopathic Hospital, dealing as it does not merely with custodial insane but with all the penumbra of "near-insane," of incipient, mild and curable cases, and with many psychoneuroses which would not ordinarily be classed among the insanities, is a somewhat broader and deeper task in diagnosis than that of the custodial institutions for the insane. The Psychopathic Hospital stands as a sort of vestibule between the community and the custodial institutions. From its meshes go back into the community numerous cases whose psychopathia is not far advanced enough to go through the interstices. Not only insanity in the narrow sense, but a variety of other conditions of the *non compos mentis* group, namely, feeble-mindedness, epilepsy, and even many forms of alcoholism come within the purview of the Psychopathic Hospital. The task of rapid diagnosis was one which had never faced the custodial institution for the insane, because to the latter flowed only cases in which diagnostic experts had made their decision outside the walls of the institution and with the concurrence of the Courts. It became necessary, therefore, to contrive more rapid methods of handling cases than had formerly been available, inasmuch as keen and mature experts were not available for the great run of cases (the Psychopathic Hospital ran the number of voluntary cases and of so-called temporary care group of cases up by the hundreds as soon as it was founded). Some provision had to be made whereby younger men could make reasonably accurate primary siftings of the cases. The rapid development of mental hygiene stole away the young men at such a rate from our staff that provision had to be made for shifting staffs of relatively inexperienced persons. The situation was not unlike that which faced the army itself at the outset of the first draft.

Mental diseases have no indicator symptoms, barring a few, and indeed a very few, so-called pathognomonic symptoms. Psychiatry was devoid of pointers, such as would be available to the specialist in the exanthems, for example. In the absence of indicator symptoms, some method had to be chosen by which every case would have every major hypothesis concerning its nosological grouping raised at some time during his hospital stay. The legal details and official regulations were such that these hypotheses had to be raised within a very short period. Early in our experience the laws and regulations were such that some kind of diagnosis permitting proper disposition of the case had to be made within four or five days. This proved to be too brief a period in

which to make proper disposition and the Temporary Care Law, under which the majority of Psychopathic Hospital cases are admitted for observation directly from the community (without court process), was modified so that a period of seven or eight days is now available. Official disposition is at present made in a total period of ten days, instead of in a total period of seven days; but in practice the external conditions of transfer to social adjustment take from two to three days, so that the total time available for group diagnosis is now a period of from seven to eight days. During this period of seven to eight days what can be done?

I assume that in private practice it may not be necessary to secure the Wassermann reaction of the serum in each and every mental case. For my part, I never feel certain of the diagnosis unless this precaution is taken. In any event, in Psychopathic Hospital practice, with the varying conditions of staff and history standard, it shortly proved necessary to get the Wassermann data from the serum in each case. Only a few of the more conservative hospital superintendents failed at first to approve this plan. The Danvers Hospital in Massachusetts and the hospitals in Michigan, under the influence of the Psychopathic Ward at Ann Arbor, had early adopted doing the Wassermann reaction of the serum as routine. Upon reflection, I found that the proper disposition of almost each and every case depended upon our securing this Wassermann data. If the Wassermann data were dubious, then a longer period of diagnosis was necessary. If the serum proved negative but there were other signs of organic disease of the nervous system, lumbar puncture was resorted to, with the diagnostic hope that the Wassermann reaction and the other reactions of the fluid would prove decisive. The practical disposition of each case I found to depend upon taking the Wassermann reaction of the serum. Accordingly, although there is no indicator symptom which is infallible or anywhere near infallible in the detection of neurosyphilis, the value of the Wassermann reaction of the serum is such that I feel entitled to place the syphilopsychoses, or mental diseases of syphilitic origin, at the head of all diagnostic consideration. This was the beginning of the plan of ordinal exclusion, the plan of diagnosis *per exclusionem in ordine*. The first thing to be excluded in the diagnosis of mental disease was, in short, syphilis.

The second thing to be excluded was, I found in practice, some form of feeble-mindedness. To be sure, the obvious imbeciles and idiots may secure their diagnosis by inspection, and not so much difficulty is ordinarily felt amongst the morons or the feeble-minded proper of the English classification. But when one came to the so-called stupids or subnormals, that we now find to lie between the morons below and the normals above, the value of the Binet-Simon tests or their analogues became extreme. One does not need to claim one hundred per cent values for these tests any more than for many another biological test. The tests are nevertheless of value. I found that in practice I needed to know for every lucid case, that is, for every case which could practically be tested metrically, the intellectual titer. Even were I dealing with such a condition as dementia precox or manic-depressive psychosis, I nevertheless found that I needed the mental test as a base line.

Thirdly, I found that the hypothesis of epilepsy or epileptic symptoms and of epileptoid phenomena is one very apt to be isolated from consideration by the tyro or even by the expert. I placed epilepsy third in the diagnostic order of exclusion partly because of the relative reliability of the clinical histories in these cases.

After Group I, the syphilopsychoses, Group II, the hypophrenoses (feeblemindednesses), Group III, the epileptoses, Group IV, the pharmacopsychoses (including mental diseases due to alcohol, drugs and poisons), I come to Group V, the group of mental diseases due to focal brain disease,—the so-called encephalopsychoses. This is the group of cases in which we unconditionally need the data of the routine neurologist's diagnosis. We need to exclude conditions of heightened intracranial pressure and conditions of asymmetry, reflexes and the like, indicating focal brain disease.

Sixthly, after Group V, the encephalopsychoses or neurologist's group, I found that in practice I was asking for the data of the internes, namely, the data which would go to make a diagnosis of a mental disease somewhere in the "symptomatic" group,—Group VI, a group I have termed the somatopsychoses.

After these I tried to exclude presenile and senile phenomena belonging in a group which I have termed, following Nascher's Geriatrics, the geriopsychoses (Group VII).

Then come the stock difficulties of diagnosis for the psychiatrist,—the diagnosis of Group VIII, the dementia precox group, which I like to term (from their main symptom as defined by Bleuler) the schizophrenoses.

After the schizophrenoses stand Group IX, the cyclothymoses, or a group including the manic-depressive psychoses and similar mental diseases.

The last of the ten well-defined groups is the familiar group (X) of the psychoneuroses including the hysterias, neurasthenias and psychasthenias, but if in the diagnostic order of exclusion one could not place one's case in any one of these ten comparatively well-defined groups, one would not throw it altogether out of the psychiatric lists, but would call it a plain psychopathia and put it in Group XI, the psychopathoses. A table of these major groups is shown on the following page.

I have spoken of the botanical and zoological analogues of this grouping in a paper read before the Neurological Association in 1917. Two words of warning are necessary concerning this analogy. The choice of the ending *osis* is obviously an attempt to get a medical analogue for the botanical ending *-aceae* or *-osae*, as in the orders *Rosaceae* and *Leguminosae*. These botanical orders are, as is well known, susceptible of splitting into genera and species. It would be an entirely superficial objection, for this account, to say that the term "species" has obtained in natural history a very special meaning which could not appropriately be given to a disease. Biologically speaking, a species is sometimes taken to mean such a group of plants or animals as are capable of breeding true to type. However, the genus-species distinction is a great deal older than natural history and is used throughout every province of logical

classification known. For example, the mineral kingdom, though without process of breeding, is in part susceptible to a classification of the genus-species sort. For that matter, it is not necessary to use the terms order, genus and species for these groupings at all. One might use entirely other distinctions, and still the process of classification might be entirely valid.

The other point which should be made is a kindred one. In zoology and botany one would ordinarily be satisfied if in the process of logical exclusion one arrived at the animal or plant which fulfilled the conditions of differentiation, but in the process of diagnosis *per exclusionem in ordine* as applied to mental disease one unconditionally needs to go through the entire list in each case.

For example, one might easily face an instance of mental disease such that the victim was a syphilitic, feeble-minded, epileptic, alcoholic old man, with focal brain disease and somatic disease, the whole contributing to his mental picture. He might conceivably have been psychoneurotic or cyclothymic in

MENTAL DISEASE GROUPS (ORDERS)

1. Syphilitic	Syphilopsychoses
2. Feeble-minded	Hypophrenoses
3. Epileptic	Epileptoses
4. Alcoholic, drug, poison	Pharmacopsychoses
5. Focal brain ("organic," arteriosclerotic)	Encephalopsychoses
6. Bodily disease ("symptomatic")	Somatopsychoses
7. Senescent, senile	Geriopsychoses
8. Dementia precox, paraphrenic	Schizophrenoses
9. Manic-depressive, cyclothymic	Cyclothymoses
10. Hysteric, psycho-, neurasthenic	Psychoneuroses
11. Psychopathic, paranoiac, et al	Psychopathoses

his life, for these conditions are doubtless consistent with a fundamental feeble-mindedness in some cases. Whether he could also have been a victim of schizophrenia (dementia precox) and still have mental phenomena attributable to all these other groups is a question. We are aware of cases that start by being feeble-minded and apparently have their schizophrenic process grafted upon them; but whether these combinations of psychoses in so multiplex a form are common or really exist is not my point. Combinations of two or three of these conditions are not infrequent. It is, therefore, stringently necessary, in the rough analysis of psychiatric cases, to make all of these major hypotheses and dismiss them or fix upon them one by one. In short, diagnosis *per exclusionem in ordine* does not necessarily exclude ten out of the eleven groups, but it does endeavor to exclude each one of at least ten of the groups. If the process has succeeded in excluding the first ten, the case, if psychiatric at all, must remain in the unresolved or ragbag group of psychopathias, Group XI, the psychopathoses. I do not intend here to enter the minutiae of psychiatric diagnosis, although in another place I have made some endeavor to describe the main genera and species of the groups above tabulated.[26] Incidentally, I have endeavored to place genera and species in the same sort of practical order so that the tyro may consider the diagnosis

of the species of syphilitic, hypophrenic and other forms of disease in arbitrary order.

It is scarcely necessary for me to insist that I do not attach great consequence to there being ten or eleven more or less major groups of mental disease. In fact, I insist that the future must interpolate or extrapolate these groups. The groups are not groups based upon clinical resemblances alone, upon anatomical disease, or upon etiology. They are practical groups devised upon what has been found to be the best practical order of exclusion of major groups of mental disease, each seeming to require a special form of handling. I have described the method in my paper entitled "A Key to the Practical Grouping of Mental Diseases." I am not sure that I would not be warranted in using the term pragmatic instead of practical, for the end and aim of these groupings is, after all, a therapeutic one. The basis for these rough distinctions is a question of disposal of the patient. If the patient belongs amongst the syphilopsychoses, then antisyphilitic therapy is indicated, or at least must be thought of. If the patient is hypophrenic, then a school for the feeble-minded, an institutional equivalent, or some form of supervision looking to the safeguarding of the community and the development of the case must be adopted. If the case is epileptic, certain special safeguards are necessary, whether the case is an alcoholic epileptic or a traumatic epileptic. The etiology and the anatomy are not at all so much to the point as the practical handling of the epileptic. So, too, with the alcohol and drug cases. In fact, the practical consequences of placing one's patient in one of the first four groups of syphilitic, hypophrenic, epileptic and alcohol or drug cases are such that I think on these practical grounds alone it would be wise for the diagnostician to consider syphilis, feeble-mindedness, epilepsy and alcohol, drugs and poisons before he comes to the minutiae. He will thus get settled in his mind many of the practical social questions of a legal, institutional and social service nature. Take the group of mental diseases due to focal brain disease. Should the phenomena of the present war show us that the traumatic psychoses, that is, psychoses due to structural brain disorder, form a practical group on a level of practical interest equal to that of the listed groups, I for one should have no objection to raising these traumatic psychoses, which I at present place under the encephalopsychoses, to a higher dignity, namely, that of the traumatopsychoses. For the moment, I seem to feel, and I suppose most of my colleagues would agree with me, that the traumatic psychoses rather resemble genera under the focal brain disease group than the true great orders of disease. Let the list be telescoped or accordeonized as you will, no damage is done to the concept-value of the greater groups of mental disease.

Again, should someone wish to consider the somatopsychoses ahead of the focal brain disease group and exclude e. g. pellagra and cardiorenal disease from a role in the given patient ahead of brain abscess, brain tumor, arteriosclerosis, and the like, I should have no objection. The point I make is that some order, not any particular order, is desirable for the tyro in diagnosis. I insist, therefore, on no particular great groups, but on the principle that

there should be great pragmatic groups of mental disease analogous to the orders of botany. I insist, again, on no particular order of exclusion, but on some order of exclusion of these groups, and above all, I insist upon subjecting each mental case, so long as indicator symptoms are so woefully absent, to the hypothesis of his possibly belonging under every one of these great groups. Indeed, I feel that he may belong in two or more of these groups.

Whither, you may ask, does the pragmatic principle then disappear? Suppose a man is both epileptic and alcoholic; shall we classify him as in the group of epileptoses or in the group of the pharmacopsychoses? All specialists will remember acrimonious discussions of this nature. Are we dealing with epilepsy or with alcoholism, or with both? Now, I find that in practice, if you couch the question pragmatically, there is rarely, if ever, any doubt into what group you wish to throw your case. Once you put the question thus: Do you wish to send this case to an institution for epileptics or do you wish to put him in an institution for alcoholics or under appropriate supervision suitable for alcoholics? There is almost never any doubt on the part of the careful physician whether his case is a case for an institution for epileptics or a case for an institution for alcoholics. The pragmatic question is forthwith settled. The academic question, whether one is an epileptic alcoholic or an alcoholic epileptic becomes a vividly practical question, when the pragmatic, that is to say, the therapeutic, question is raised. I find that this kind of consideration matures the tyro in psychiatry very fast.

SUMMARY

1. The writer apologizes for a communication on Medical Logic in general when he is only a psychiatrist and but recently a pathologist. His excuse is the necessity for reasonably accurate snap diagnosis in the sifting problem of the psychoses, psychoneuroses and psychopathias, as they flow through the Psychopathic Hospital clinic in Boston.

2. The medical student is found destitute of the ability to define entities and symptoms. The textbooks in medicine, especially the single volume textbooks, rather tend to make the student believe that diagnosis is observation. In point of fact, diagnosis is not observation, though it requires and indeed stands or falls by accurate observation.

3. Da Costa and his successors have lauded so-called direct diagnosis to the skies and Da Costa rather decried indirect diagnosis by exclusion as a tedious process. An example is cited from Da Costa which shows how relatively simple the classical diagnoses of general medicine are beside those of psychiatry.

4. It seemed that diagnosis by exclusion ought to be rehabilitated. An examination of recent research work in logic indicated that higher and more complex methods than those of observation had become necessary in science. For example, Cabot and Herbert French have attempted to profit by the statistical method, which again, though it requires reasonably accurate observation, is not in itself a method of observation at all. Yet Cabot's statistical fre-

quency tables possess a certain diagnostic value. But the student is often misled by the brilliancies of so-called observational diagnosis in a clinic. Here diagnoses are often rendered on inspection by a process akin to the recognition of a fruit as an orange, or an automobile trouble as "the engine is skipping." This process is not diagnosis, it is a process of recognition that may receive a simpler term *gnosis*.

5. The offhand snap diagnostic work at the Psychopathic Hospital indicated that we were in practice relying upon the successive exclusion of certain great disease groups in a certain definite order.

6. A study of Royce's "Summary of Recent Researches in Logic" shows how an organized combination of theory and experience is the higher logic to which the more complicated sciences must resort. Royce himself mentioned psychiatry as a science about to climb out of the classifying era into the era of logical order, that is, of the organized combination of theory and experience. Such a dictum that "disease is life under altered conditions" appears now childishly simple. The idea that disease is a matter of an organism plus a germ was found to be altogether too simple when in the nineties of the last century the concepts of immunology were developed.

7. Those departments of medicine in which the presenting symptom of Richard Cabot is of value are lucky departments. Those departments of medicine in which the indices of disease, or indicator symptoms of the elder writers are available, are also fortunate departments in comparison with psychiatry. In mental disease there are exceedingly few indicator symptoms.

8. Hence the need became apparent of a process of exclusion of great groups or phenomena in a certain definite order, so that nothing of large significance should evade consideration. To avoid the tediousness of exclusion, complained of by Da Costa, the phenomena of disease had to be logically grouped in certain great groups, and the process types of diagnosis in the books may be counted as six or eight, according to definition.

9. In the body of the paper, a special statement was made about each of these process types: Inspection (regarded as not really diagnosis but as merely recognition of gnosis). Expectation, a newly named but frequent method (far older than Micawber). Induction, *Ex juvantibus, Ex nocentibus* (three methods in which in no very rigorous way experiment is used) and three methods of diagnosis by comparison are successively discussed.

10. The ninth method, diagnosis *per exclusionem in ordine*, is in one sense a minor modification of the old method of diagnosis by exclusion. It is of value in departments of medicine where there are no indicator symptoms, and where the so-called presenting symptom would merely indicate some kind of mental disease.

11. The general application of the method of diagnosis *per exclusionem in ordine* in the field of mental disease is demonstrated in the eleventh group of mental diseases into which most of the phenomena may be pragmatically cast. The groupings are not by clinical resemblances, by anatomical attack or by etiology. The distinction is a pragmatic and therapeutic one and will naturally

tend to become more and more etiologic as the causes are determined. But in the field of mental disease, causes are so apt either to be unknown or to be multiple that etiologic classification on any simple basis such as that of the infectious diseases is practically inconceivable.

12. It is hoped that other departments of medicine (where diagnosis is raised above the level of mere recognition) and where there are few or no pathognomonic or indicator symptoms, will find it to their advantage to set up a method of diagnosis *per exclusionem in ordine*, the great groups or orders being always determined on a pragmatic basis. In the body of the paper are given the general designations of the ten great groups of mental diseases, with the eleventh residual group.

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THE BACILLUS INFLUENZÆ IN SINUSITIS AND MENINGITIS*

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SINCE the discovery by Pfeiffer of the Bacillus influenzæ during the influenza pandemic of 1892, a great deal of work has been published showing the presence of this bacillus as the probable etiologic factor in a number of the sequellæ of clinical influenza and other allied conditions. Pfeiffer's work is well reviewed by Scheller,[1] in which he gives an excellent resumé of all that was known of the organism up to that time. Pfeiffer was able to demonstrate the Bacillus influenzæ in the sputum of a large percentage of his cases of clinical influenza during the early stages of the disease but during the later stages it had disappeared entirely. Davis[2] has more recently (1908) reported forty-one cases of clinical influenza in which his findings were quite at variance with those of Pfeiffer, in that he was unable to demonstrate the organism in the sputum of but seven of his forty-one cases, and that in these he found the bacilli only during the later stages of the attack. The earliest he found them was on the fourth day, the average time being much later.

Of greater interest perhaps, than the presence of Bacillus influenzæ in the sputum, is its presence in the accessory sinuses of the respiratory tract and in the spinal fluid of cases of influenzal meningitis. During the last year two instances of sinusitis without meningitis and two which were followed by meningitis have come to our laboratory. I shall make these the basis of this report.

CASE HISTORIES

Case I.—*Influenzal Meningitis.*—Baby S. Male. Age ten months. Patient of Dr. D. H. Boyd. Children's Hospital, Pittsburgh. The patient though still well nourished showed evidences of rapid loss of weight. Family history and past history negative. The patient was brought into the hospital April 24, 1917, in an unconscious condition. The present illness had begun about four weeks before with pain and swelling of the right knee, followed two weeks later by pain and stiffness in the shoulders. There was slight improvement until two weeks later when he became irritable, began vomiting and was unable to retain his food. Physical examination on entrance to the hospital showed that the patient remained in any position in which he was placed, with eyes turned toward the right. Every evidence of meningitis was present except a positive Koernig. Further physical examination was negative except for slight dullness and increased breath sounds both anteriorly and posteriorly over the right lung more marked at the base than elsewhere. A few moist rales were also present. A diagnosis of meningitis was made. Lumbar puncture yielded 40 c.c. of turbid spinal fluid under pressure. The cell count was 276 per c.mm. and smears showed several organisms which appeared to be gram-negative cocci, some seemed to be in chains and were not typical of meningococci. There is no record of cultures having been made on the spinal fluid during life. Daily lumbar punctures showed the same type of fluid until death occurred on April 27, 1917. The body was brought to the Singer Laboratory for autopsy.

Autopsy Report.—Autopsy (Drs. Plumer and Allison). The body was one of a well-developed and moderately well-nourished white, male child apparently about one year old. The pupils were unequal, the abdomen was retracted and the right knee was swollen. No other unusual conditions were noted externally. The thymus gland was relatively small. The other thoracic and abdominal organs were greatly congested and otherwise

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appeared negative. The important pathologic changes were contained within the cranial cavity and spinal canal.

Brain.—The dura was distended from internal pressure. The cerebrum was covered with a yellowish fibrinous exudate which formed a part of a membrane extending more or less completely over all of the brain surfaces. Over both upper and lower surfaces of the frontal lobes the membrane was so thick and shaggy that the vessels were entirely obscured. The Sylvian fissures were completely filled with the exudate. Over the parietal and occipital lobes the membrane was not so thick and the greatly congested pial vessels stood out prominently. About the optic commissure and infundibulum and over the cerebral peduncles, pons, medulla and lower surfaces of the cerebellum the exudate was again very thick. The left lower cerebellar surface was covered with a somewhat thicker layer of fibrin than the right and the superior surfaces of both cerebellar lobes were practically free. The general appearance and the boggy feel of the cerebrum suggested the

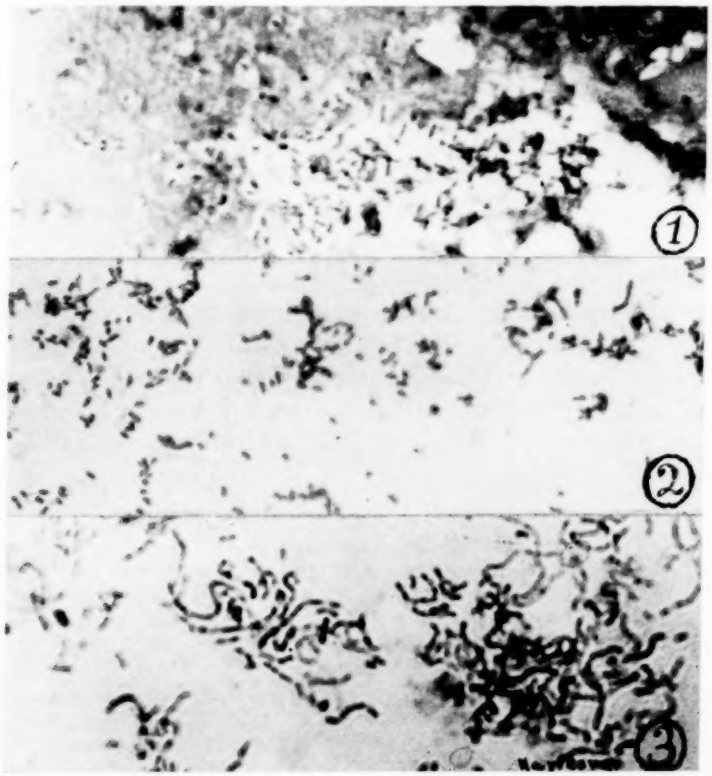

Fig. 1.—Direct smear of sputum showing influenza bacilli. 2. Forty-eight-hour culture showing early division forms and spirals. 3. Seventy-two-hour culture showing filamentous involution forms.

presence of fluid in the lateral ventricles but the brain was placed unopened in a hardening fluid. The cord was covered with a similar membranous exudate. Both middle ears contained yellow pus.

Microscopic Description.—Microscopically the meninges were seen to be covered with a sero-fibrino-purulent membrane of varying thickness. All of the sections showed the presence of an abundance of fibrin which was of the filamentous nonhyaline type, the strands of which were widely separated by serous and cellular exudate. In the thicker portions the cellular elements predominated with a high proportion of polymorphonuclear cells; many plasma cells and phagocytic endothelial cells also being present. A few short gram-negative bacilli were made out. These were both intra- and extracellular. The smaller vessel walls were swollen and infiltrated with leucocytes. The connective

tissue cells of the pia were swollen and edematous. The brain substance proper presented no evident changes beyond a marked edema.

The lungs were edematous and the bronchioles were filled with an acute exudate, which was composed chiefly of leucocytes and fibrin and which contained very small gram-negative bacilli and a few other bacteria. The kidneys showed marked tubular degeneration, congestion and edema. The other organs were not remarkable.

Bacteriological Report.—Direct smears from meningeal exudate were negative. Cultures were taken at autopsy from the cerebrospinal fluid, lepto meninges, base of the brain and from the middle ears. The middle ears and the meningeal cultures contained a predominance of very fine short gram-negative bacilli, which at first were difficult to distinguish from diplococci. This organism was also found in pure culture in the spinal fluid. It grew only on blood agar and required forty-eight hours for its development. Since it was recovered in pure culture from the spinal fluid at autopsy it is reasonable to assume that it was the same organism which was found in the spinal fluid before death. This organism was in every respect identical with the influenza bacillus. There were a few gram-positive cocci recovered from the meninges and also from the mastoid cells. These were staphylococci and were perhaps a contamination from opening the cranial cavity as they were only very few in number.

CASE II.—*Influenzal Meningitis.*—Baby H. Patient of Dr. L. C. Fausold. A well-nourished male child ten months of age. The father said that the child had been strong and well until a short time before the present illness when it developed a cold which lasted several days and was followed by a profuse discharge from the nose and from the left eye. There was also a marked swelling developed over the region of the left maxillary sinus. These had subsided somewhat when the patient (November 21, 1917) began to show signs of meningeal irritation. By the twenty-third definite symptoms of meningitis were present. About 30 c.c. of cerebrospinal fluid was withdrawn by Dr. Fausold who stated that it was under great pressure. The fluid was very turbid, so much so that a heavy precipitate had formed in the bottom of the tube by the time it was received at the laboratory. A cell count was not made on account of the extreme turbidity. Direct smears were made from the sediment and stained by Gram's method, which showed the cells to be practically all of the polymorphonuclear type. Throughout each microscopic field extracellular and occasionally intracellular gram-negative bacilli were found which varied greatly in size. The majority of these bacilli were slightly larger than the average influenza bacillus and gave the appearance of the leptothrix group of organisms. Cultures of this organism proved to be a pure culture of Bacillus influenzæ. Lumbar punctures were done daily for several days giving temporary relief and the spinal fluid became much less turbid. The patient appeared greatly improved for about a week or ten days but became very much worse and died December 5, fourteen days after development of symptoms. Pure cultures of the same organism were recovered from the fluid obtained at subsequent punctures.

CASE III.—*Frontal Sinusitis.*—Mr. H. C. Patient of Dr. Robert Milligan, Allegheny General Hospital. A young white man, twenty-three years of age. Occupation, engineer. Family history and past history negative. Present illness began in February, 1917, with an attack of grippe. This lasted several days and after he was up he noticed a swelling over his upper right eyelid. This became very painful and his physician incised it. A large amount of pus was evacuated and continued to drain through the incision, so that a sinus was formed. He finally sought the services of an ophthalmologist and was treated with injections of silver nitrate without benefit. On July 7, 1917, the sinus was curetted and some pieces of necrotic bone removed. The discharge continued and he was transferred to the service of Dr. Milligan in September. Attempts were made to institute drainage from the frontal sinus through the nose by doing, first a turbinectomy and later a high submucous resection of the septal plate. These methods each failed to relieve the condition and on November 6 the discharging sinus was incised, the anterior wall of the frontal sinus removed, thorough light curettage done, the wound packed and drainage established both externally and through the nose. The discharge remained very profuse despite the fact that the wound was being irrigated two or three times daily alternating with a weak solution of potassium permanganate and distilled water. A culture was made at this time which showed almost pure culture of Bacillus influenzæ with an occasional colony of hemolytic streptococci. A vaccine was prepared from this and given at four-day intervals. It produced a rather severe local reaction especially after the first few injections. There was decided improvement in the patient's general condition and lessen-

ing of the discharge after the second injection. Although there was still a slight amount of discharge from the wound it was improving and the patient was dismissed from the hospital December 19, 1917. At that time cultures from the pus were negative for Bacillus influenzæ.

CASE IV.—*Frontal Sinusitis.*—Patient of Dr. Milligan. Allegheny General Hospital. A white man, aged thirty-two years. Occupation, toolmaker. Family history negative. Past history negative except for an apparent susceptibility to colds, which he had had three or four times during the last year. The patient says that two years ago he began to have pain over the left side of the face; he had a tooth extracted but this failed to give relief. Since that time the pain has been intermittent. The pain would start at the inner canthus of the left eye and spread over the left side of the face and head. Nothing had been done surgically to relieve the condition, but he had seven years previously had a submucous resection of the nasal septum on the left side. During the past few months he had had the frontal sinus probed through the nose several times in an attempt to establish thorough drainage through this route. Each probing was followed by prompt relief but it was only temporary. On November 20, 1917, an incision was made over the left superciliary ridge, a trephine done and a small portion of bone forming the anterior wall of the frontal sinus was removed. Light curettage of the frontal sinus was done, the anterior ethmoid cells opened and the superior turbinate and bulla ethmoidalis removed and a gauze drain passed down through the opening thus formed. The external wound was closed and the drain allowed to remain in position two or three days. No further local treatment was given except necessary dressings. A culture taken from the frontal sinus at operation showed a predominance of Bacillus influenzæ with a few staphylococci and streptococci. A vaccine was prepared for this patient and given as in Case III, but the results were not so encouraging.

The bacteriological findings in these four cases were interesting in that they represented two different types or forms of the Bacillus influenzæ. First, the small short "text-book" type and second the long filamentous or streptothrix-like forms called by Pfeiffer "scheinfädenbildung" or involution forms. Attention has also been called to these two forms by Wollstein,[3] Henry,[4] Ritchie[5] and Bhat.[6] Wollstein states that the shorter forms which she used were obtained from the sputum of influenzal patients and the longer forms from patients with influenzal meningitis. She found the long ones to be of much higher pathogenicity than the shorter ones.

In the four cases reported above, the short forms were isolated from Cases I and IV and the longer ones from Cases II and III. In each of the first three cases it required forty-eight hours for the development of the characteristic pin point or dewdrop colonies on blood agar while in the last case they developed in twenty-four hours. This latter occurrence may have been due, as others have suggested, to the presence of the streptococcus and staphylococcus associated with the Bacillus influenzæ. A point against this is that after it had been isolated in pure culture the growth was equally as rapid. All of the cultures showed a tendency for the colonies on blood agar to remain discrete. Each failed to grow on any of the ordinary media except blood agar and litmus milk, the latter being alkalinized in about six or seven days. The short forms in Cases I and IV retained their original morphology as long as they were kept on culture media, which was for a period of several weeks. There was no tendency toward the formation of the longer or involution forms. The shorter forms predominated in Cases II and III when the cultures were first isolated, but after the first transfers the long filamentous forms began to appear and were soon in the majority with only a few of the short ones remaining. It was noted that these long filaments were generally found on the lower part of the culture tube near the water of condensation, which suggested that the moisture of the media might have some effect on their production. Transfers were therefore, made from a culture containing the long type, to blood agar which had been well dried for several hours in a paraffin oven. Colonies developed on this medium in forty-eight hours as on the fresh moist medium but smears from these showed the bacilli to be practically all of the short variety. Transfers to the moist blood agar showed a return to the long filamentous forms, showing fairly conclusively that we were dealing with two phases of the same organism and not with different organisms. There seems to be a definite relationship between the development of influenzal meningitis and infections of the frontal and maxillary sinuses and mastoid cells, a point previously mentioned by Cohoe[7] and Ritchie. In one of our cases the meningitis was preceded by an infection of the mastoid cells and in the other by an infection of the maxillary sinus.

SUMMARY

In all cases of meningitis, either mild or severe, of indefinite etiology it is advisable to centrifuge the spinal fluid and culture it on various media, always using blood agar. Observations on this should be made for at least forty-eight hours before a negative report is made.

The presence of gram-negative bacilli in direct smears or on cultures from cerebrospinal fluid or from the accessory sinuses of the respiratory tract should be looked upon as probable Bacillus influenzæ. This is especially true when long filamentous forms are present.

There are probably two types of Bacillus influenzæ as suggested by the cases reported here; the one which retains its original short bacillary form indefinitely on artificial media and the other which readily develops filamentous forms after a few days on moist blood agar.

Sinus infections with the Bacillus influenzæ should have early and adequate drainage to prevent the danger of a complicating meningitis.

NOTE.—Since the completion of the above work,* Major H. E. Robertson of the American Expeditionary Force in France, has reported the recovery of B. influenzæ from the accessory sinuses of fourteen cases at autopsy: seven times out of eight, cases of influenzal tracheobronchitis; six times from patients dead from other infectious diseases; and twice from men dying of accidental causes. Major Robertson did not go into the cultural characteristics nor morphological differences of the bacillus. (S.R.H.)

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THE COMPARATIVE VALUES OF SOME LOCAL ANESTHETICS*

By Herbert C. Hamilton, Detroit, Mich.

NOVOCAINE, while conceded to be somewhat less effective in practice than cocaine, has gained a reputation for effectiveness which, taken along with its stability in solution when heated to sterilize, its lower toxicity, and its freedom from habit-forming effects, has made it second to none in its general applicability. While it is true that most of the defects of cocaine can be overcome by one means or another the disappearance of novocaine from the market has been generally regarded as a distinct loss.

A recent addition to the list of local anesthetics is apothesine, which has proved to be not merely a substitute for novocaine and cocaine but a product worthy of closest investigation. Unfortunately, in a series of experiments by Sollmann[1] in which he examined some of the most important local anesthetics this product was passed over as of minor importance.

The reason advanced by Sollmann for reopening an investigation of local anesthetics namely "the wish to select 'the best'" is sufficient reason for this publication, with the added incentive that while his work is apparently comprehensive, covering as it does the efficiencies of a number of substances by five different methods of valuation, the whole field is not fully covered, since apothesine is included in the tests of only two of the five series.

The first series of his experiments, and the first one appearing in complete detail,[2] is that describing the comparison of a number of local anesthetics on the sciatic nerve of the frog. One would assume from reading the first article that apothesine had not come to the author's attention.

In two subsequent test-methods, however, it is included—in the cornea test and in the intracutaneous test. Based on the results obtained by the first of these two methods he concluded that novocaine and apothesine are inefficient relatively to cocaine, although apothesine is 100 per cent more active than novocaine. In the intracutaneous test his results would indicate that novocaine is fully equal to cocaine while apothesine is only one-eighth as efficient.

Since Sollmann's experiments led him to conclusions radically different from those which we have observed the subject is reopened to include the comparison of apothesine with other anesthetics by three of the methods he applied and to point out what are evidently errors in his work.

As in Sollmann's paper this publication does not touch on the toxicity since there are different interpretations to be placed on results obtainable by almost any method. The important feature in this respect is that apothesine is only one-fifth as toxic as cocaine by subcutaneous injection into guinea pigs and that in relatively large doses no systemic effects have been in evidence. Local irritation, too, is a clinical problem and may logically be omitted from this discussion.

As to the relative merits of the different methods of examination of local

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anesthetics this too must be left to the ultimate judgment of the clinician. The use of a new anesthetic is necessarily governed by its relative efficiency, first of all as shown by laboratory tests but finally by observation of its action in practical use.

Among the laboratory tests that have been devised for investigation of local anesthetics there are three, each of which appears to have a very direct bearing on the clinical application of these substances, namely—the intracutaneous, comparable to infiltration anesthesia; the nerve trunk anesthesia, comparable to nerve blocking or conduction anesthesia; and surface anesthesia—the mucous membrane of the eye, nose and throat—reproduced by application to the frog's foot or to the cornea.

If the results of testing the different local anesthetics by the different methods agreed relatively, this would show that comparison by any one of the methods would give the relative efficiencies. That this is not true, however, is apparently shown by observing the varying ratios obtained by both Sollmann and ourselves. The laboratory results are therefore only suggestive, and do not absolutely demonstrate the clinical value of a local anesthetic.

In the following experiments the hydrochlorides of each of the local anesthetics tested were used in every case, no experiments having been conducted after neutralization. Experiments with mixed anesthetics were also omitted as having no direct bearing on the object of the paper.

MOTOR NERVE ANESTHESIA

The method most commonly used for testing the value of a local anesthetic where exact data is desirable, is to apply the anesthetic to the sciatic nerve of the frog, the nerve being separated at its point of branching from the spinal column. The objection has been made that this is a determination of motor nerve anesthesia only and no evidence of efficiency on the sensory nerves. It has been demonstrated, however, that the sensory nerves are the first to be anesthetized[3] and therefore a measure of motor nerve anesthesia is a fair indication that the sensory nerves are at least equally anesthetized. Objection has also been made that this method is very different from the practical use of anesthetics, but on this point, too, there are counterbalancing reasons which give the method practical value for measuring anesthetics. This test shows at once the nerve blocking value such as results from subcutaneous and subdural injections and as this is one of the uses of local anesthesia, its measurement is of primary importance. This method also meets one of the requirements of physiological testing in its accuracy of measurement, the exposed nerve can so easily be irritated to determine the degree of anesthesia when either the strength of solution or the length of time is the measuring factor. The accuracy of measurement is not affected by the factors which may affect the intracutaneous method, one of which is the pressure of the solution and another its character, such as tonicity, concentration, irritation, diffusibility.

As a sole method of valuing local anesthetics it would fail to give a true picture, but taken as one of several methods, especially along with that of subcutaneous administration the nerve blocking action is undoubtedly of primary importance and deserves especial consideration.

This phase of the subject has been so thoroughly covered by other investigators that no further description is necessary and only additional data or materially different results furnish an adequate reason for further publications.

While working with the intent to verify or disprove Sollmann's results the method followed was varied to the extent that no work was carried out with the high dilutions he employed, these having no practical bearing on the subject.

TABLE I

ANESTHESIA AS SHOWN BY RESPONSE TO CURRENT AFTER MINUTES

SUBSTANCE	DILUTION %	0	5	8	10	12	15	20	25
Cocaine	0.5	–	–	±	±	+			
		–	–	±	±	±	±	±	+
		–	–	±	±	±	±	+	
Cocaine	1.0	–	–	±	+				
		–	–	±	±	+			
		–	–	±	±	+			
Novocaine	0.5	–	–	±	±	±	±	+	
		–	–	–	±	±	±	±	+
		–	–	±	±	±	±	+	
Novocaine	1.0	–	–	±	±	+			
		–	–	±	+				
		–	–	±	±	+			
		–	–	±	±	+			
		–	–	±	±	+			
Apothesine	0.5	–	–	±	±	±	+		
		–	±	±	±	+			
		–	–	±	±	±	±	+	
		–	–	±	±	+			
		–	–	–	±	±	±	±	+
Apothesine	1.0	–	–	±	+				
		–	–	±	+				
		–	±	+					
		–	–	±	+				
		–	–	±	±	+			
KCl	0.5	–	–	–	–	±	±	±	+
	1.0	–	±	±	±	+			

TABLE II

TIME IN MINUTES REQUIRED FOR COMPLETE ANESTHESIA OF THE WHOLE LENGTH OF THE SCIATIC NERVE

	.05% SOLUTION	1% SOLUTION
Cocaine	12-25	10-12
Novocaine	20-25	10-12
Apothesine	15-25	10-12
Potassium Chloride	25	12

It was planned to use such dilutions only as would bring about complete anesthesia in five to ten minutes but the lower time limit was in no case sufficient with the dilutions used.

The irritation was produced from a three cell battery through a secondary with 5000 windings adjusted to a point where the current is just perceptible on the tongue.

The sciatic nerve of the frog is dissected, leaving a small piece of the bone

attached, for convenience in handling, and having the whole muscle below the knee skinned but otherwise intact.

After determining that its response to stimulation is good, the whole nerve-muscle preparation is immersed in the solution, testing frequently after five minutes to determine when anesthesia begins and its progress. It will be observed that no account is taken of certain features which have formed an important part of the reports of other investigators, namely, the response to varied degree of current, the response from application of stimulus to different portions of the nerve, the exact beginning of paralysis, its duration or the recovery. While these factors are not unimportant this series of tests was made primarily to compare the efficiency of several local anesthetics, and for this purpose, one end point may be considered as good as another, other things being equal. The end point chosen was therefore that dilution which would paralyze the motor nerve all the way to its disappearance into the tissue below the knee, in a period of approximately ten minutes. However, for comparison and as evidence of different degrees of anesthesia records of other times and of other dilutions are included.

In the table, — means practically no degree of anesthesia, ± means partial anesthesia in the sense of progress along the nerve, + means complete anesthesia except the nerve just at its disappearance into the tissue of the leg.

From Table I the efficiencies of the four anesthetics are apparently so nearly equal that for all practical purposes their values by this method may be taken as equal, as shown by Table II which summarizes the results.

Comparison of these results with those of Sollmann shows that there is absolute agreement in ratio so far as each of us carried our experiments but that the efficient concentrations used are somewhat different. This is probably due to the selection of different constants and not to errors on either side.

The added data on apothesine is valuable, since the virtual agreement on the others points to a probable agreement on this substance.

SURFACE ANESTHESIA

The method is that of Gradenwitz[5] who first applied it as a means of determining the relative values of local anesthetics. The brain, medulla and heart of the frog are removed and the blood washed out to prevent general absorption of the substance which is being tested. In applying this method, one leg, after removing excess moisture, is dipped into the diluted anesthetic for 1 minute, after which it is laid in a vessel containing cold water but with the legs not immersed and separated so that none of the anesthetic touches the control leg. At five minute intervals both feet are dipped into a weak solution of hydrochloric acid (about 1/5 per cent) and the behavior closely observed. When no anesthesia has taken place both legs are withdrawn with equal promptness while as anesthesia progresses the treated leg is more slowly withdrawn until on complete anesthesia it is not withdrawn at all while the control leg reacts as promptly as at first. After each stimulation both legs are dipped in water to remove any adhering acid.

The objection has been raised that there is no direct relationship between this method and clinical practice; on the other hand the frog's skin being al-

ways moist is in a sense comparable to the mucous membrane and, in this respect, is an experimental method for obtaining relative values for mucous membrane anesthesia. Besides, it is a method with a reaction susceptible of quite exact measurement and as such takes its place as a valuable pharmacologic assay method for establishing relative values. The values so obtained may not be capable of direct application as has been stated about other methods but without question, they are not to be ignored in assigning the real position of a local anesthetic.

TABLE III

SUBSTANCE	DILUTION %	TIME AND RESULT OF OBSERVATION 5	10	15	20	25	30	35	40	45
Cocaine	2	+	+	+	+					
	2	+	+	+	+			0		
	1	+	+	±			0			
	1	+	±	±	±	±	±	±	0	
	½	±	±	±	±	±	0			
	½	±	±	±	±	±	±	0		
	⅔	–	±	±	±	±	±	±	±	0
Novocaine	2	–	±	±						
	2	–	±	±			0			
	2	–	±	±			0			
	3	–	±	+±	±	+±	+±	+	0	
	3	–	–	–	±	±	±	±	+±	
	3	–	±	±	+	0				
	3	–	±	±	±	+±+	0			
Apothesine	2%	0	±	±	±	+	0			
		–	±	±	–	0				
		±	±	±	±	±	±			
Apothesine	3	–	±	±	±	+±+	+	+	±	
	3	–	±	±	±	±	+	0		
	3	±	±	±	±	±	+	+	0	
	3	–	±	±	±	0				
KCl	1	–	±	±	–	–	0			
	2	–	±	±	±	±	–	0		
	3	+	+	+	±	±	±	±	0	
	2½	±	±	±	±	±	±	0		

SUMMARY OF TABLE IV

SUBSTANCE	EFFECTIVE DILUTION	RATIO OF EFFECTIVENESS
Cocaine Hydrochloride	1 per cent	1
Novocaine	3 " "	⅓
Apothesine	3 " "	⅓
Potassium Chloride	3 " "	⅓

Table III shows the detailed results in which equally prompt withdrawal of the legs is represented by —, progressive anesthesia by ±, while complete anesthesia of the treated member only is represented by +. When neither leg will respond to stimulation this condition is represented by 0.

Comparing these relative efficiencies with those obtained by Sollmann it is seen that he found it necessary to use a solution of novocaine six times as strong as that of cocaine as against one three times as strong in Table III. Also that of KCl, the efficient strength was twelve times as great as for cocaine against three times in Table II.

INTRACUTANEOUS METHOD

This method has the distinct advantage of most nearly duplicating one of the important uses of a local anesthetic since it is carried out in a way almost identical with that in clinical practice. Particular care was taken in the tests tabulated below to prevent the unintentional prejudice which knowledge of what was injected might have.

The injections were made by a practicing physician into the forearms of the subjects, who were asked to respond only when pain was felt when a needle prick was made on the anesthetized area or the adjacent skin.

EXPERIMENTS ON FIRST SUBJECT (H. C. H.)

First Series

	AMOUNT	DILUTION	RESULT
Cocaine	0.25 c.c.	1-500	Complete
Novocaine	0.25 c.c.	1-200	Complete
Apothesine	0.25 c.c.	1-200	Complete
Phys. Salt Sol.	0.25 c.c.		No anesthesia

Anesthesia was so complete that no distinction could be drawn between the different injections. The second series was therefore made with the same ratio of strengths but each reduced to half that in the preceding series.

Second Series

	AMOUNT	DILUTION	RESULT
Cocaine	0.2 c.c.	1-1000	Complete
Novocaine	0.2 c.c.	1-400	"
Apothesine	0.2 c.c.	1-400	"

In this test while anesthesia was complete in every case it seemed more persistent in the area injected with apothesine and in the next series the strength of the latter only was changed.

Third Series

	AMOUNT	DILUTION	RESULT
Cocaine	0.2	1-1000	Complete
Novocaine	0.2	1-400	Complete
Apothesine	0.2	1-800	Complete

In this series the anesthesia was as nearly identical as impartial observation could recognize.

The experiments were continued the next day on the same subject.

In the data below an attempt is made to indicate the degree of anesthesia and its duration by the number of plus signs.

First Series

	AMOUNT	DILUTION	RESULT
Cocaine	0.2 c.c.	1-1000	++++
Novocaine	0.2	1-500	+++
Apothesine	0.2	1-1000	++++
	Second Series		
Cocaine	0.2	1-2000	++
Apothesine	0.2	1-2000	+
	Third Series		
Cocaine	0.2	1-2000	++
Apothesine	0.2	1-1500	++

The above injections were made with not to exceed a minute interval between those of a series.

The results of these tests are summarized in Table V.

TABLE V

SUBSTANCE	DILUTION	RATIO
Cocaine	1-2000	1
Novocaine	1-1000	½
Apothesine	1-1500	¾

Experiments on a second subject (M. W.) were carried out, the degree of anesthesia being indicated roughly by the number of plus signs.

EXPERIMENTS ON SECOND SUBJECT

First Series

	DILUTION	RESULT
Cocaine	1-2000	+++
Novocaine	1-1000	++
Apothesine	1-2000	+++
	Second Series	
Cocaine	1-3000	++
Novocaine	1-2000	+
Apothesine	1-3000	++
Novocaine	1-1000	++

These results may be summarized in Table VI.

TABLE VI (M. W.)

	DILUTION	RATIO
Cocaine	1-3000	1
Novocaine	1-1000	⅓
Apothesine	1-3000	1

On a third subject (W. E. K.) the results were as follows:

EXPERIMENTS ON THIRD SUBJECT

First Series

	DILUTION	RESULT
Cocaine	1-3000	+++
Novocaine	1-1800	++
Apothesine	1-3000	+++

Second Series

Cocaine	1-4000	++
Novocaine	1-2000	+
Apothesine	1-4000	++

TABLE VII (W. E. K.)

SUMMARY ON THIRD SUBJECT

SUBSTANCE	DILUTION	RATIO
Cocaine	1-4000	1
Novocaine	1-1800	less than ½
Apothesine	1-4000	1

EXPERIMENTS ON FOURTH SUBJECT (L. W. R.)

First Series

	DILUTION	RESULT
Cocaine	1-2000	+++
Novocaine	1-1000	++
Apothesine	1-2000	+++

Second Series

Cocaine	1-3000	++
Novocaine	1-1800	++
Apothesine	1-3000	+

Third Series

	DILUTION	RESULT
Cocaine	1-4000	+
Novocaine	1-1500	++
Apothesine	1-4000	+

Fourth Series

Cocaine	1-3000	++
Apothesine	1-3000	++

Summarizing these results the ratios are shown in Table IX.

TABLE VIII

SUMMARY OF AVERAGE RESULTS BY INTRACUTANEOUS ADMINISTRATION

SUBSTANCE	RATIO
Cocaine	1
Novocaine	$1\frac{1}{24}$
Apothesine	$1\frac{5}{16}$

TABLE IX (L. W. R.)

SUBSTANCE	DILUTION	RATIO
Cocaine	1-3000	1
Novocaine	1-1500	½
Apothesine	1-3000	1

The results of the intracutaneous administration of the three local anesthetics summarized above, carried out as they were on four different persons prove conclusively two points, (1) novocaine is about one-half as efficient as cocaine, (2) apothesine is practically equal to cocaine in anesthetic value. Sollmann's conclusions from his test by this method, namely, that novocaine is equal to cocaine, and apothesine one-eighth as efficient are evidently incorrect. It is impossible to explain this discrepancy. Novocaine anesthesia is

well known to be less permanent since most observers have noted quick recovery. This, however, was not the factor in these tests since the time of recovery was only incidental in importance as compared with the degree of anesthesia from the high dilutions.

In the introduction it was stated that since tests of local anesthetics by different methods do not show entire agreement, they can be taken as only suggesting and not demonstrating the clinical value. Viewed in another way, however, it may be said that these tests demonstrate comparative efficiencies in the particular method of applying the substance.

That both novocaine and apothesine are inferior to cocaine by surface application agrees with clinical evidence which has demonstrated cocaine to be exceptionally rapid in its absorption from mucous surfaces. Braun.[4] The comparative efficiencies of cocaine and novocaine by intracutaneous injection also duplicates the opinion generally held that the latter is less efficient. On this point, Braun[4] states: "Experience and experiments have, however, shown that by doubling the dose of novocaine so as to make it as effective as cocaine, and at the same time by adding certain substances which will be described in the next chapter (suprarenin) novocaine has become an ideal anesthetic for injection of tissues and has made cocaine unnecessary." It may be assumed therefore that this method correctly measures the efficiency of apothesine as well as those of cocaine and novocaine. Verification of the motor nerve method can not be cited at this time.

Based on the foregoing results it is evident that from every point of view apothesine is equal to or exceeds novocaine as a local anesthetic and in some respects is not less efficient than cocaine. We can therefore be assured of supplies of an efficient product, independent of German patents or controlled United States laboratories operating under license to German patentees.

The author's appreciation is extended to Dr. A. W. Lescohier, who carried out the intracutaneous tests and recorded his observations; also to three associates who by their courtesy made more data available.

TABLE IX

SUBSTANCE	METHOD	GRAPHIC ILLUSTRATION OF EFFICIENCIES	RATIO
COCAINE	Motor Nerve	═══════	1
	Surface	----------	1
	Intracutaneous	++++++++++++++++++++++++	1
NOVOCAINE	Motor Nerve	═══════	1
	Surface	----------	⅓
	Intracutaneous	++++++++++++	½
APOTHESINE	Motor Nerve	═══════	1
	Surface	----------	⅓
	Intracutaneous	++++++++++++++++++++++++	1

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[5]Gradenwitz: Ber. klin. Wchnschr., 1899; xxxvi, 76.

LABORATORY METHODS

SIMPLIFIED GAS ANALYSIS

By J. J. R. Macleod, M.B., Toronto, Canada

NO. II. BURETTE WITHOUT STOPCOCKS FOR GAS ANALYSIS

FOR purposes of teaching, as well as for occasional use in clinical practice, the usual types of gas burette are unsuitable because of the care and attention that has to be given them in order to prevent "freezing" of the stopcocks. Other objections to stopcocks are that they are liable to leak unless well ground, and they add considerably to the cost of the apparatus. The increasing necessity of gas analysis in medical diagnosis and in research makes it important that simple and reliable apparatus be available.* Such an apparatus can be constructed by using screw clips in place of stopcocks, provided some means be taken to adjust the gas pressure in the burette after the screw clips have been tightened. This can be accomplished by the use of the "pressure adjuster" described below.

Another difficulty which the inexperienced constantly meet with in using gas burettes of the usual pattern (Haldane's) is in preventing the strong alkaline solution from running up the narrow tubing which connects the burette and absorption bulbs. This accident delays the analysis, since all traces of the alkali must be removed from the burette and mercury before proceeding with the analysis, and moreover the alkali, if not removed, eats its way around the stopcock, and causes etching of the glass and "freezing." In the following apparatus this danger is guarded against by inserting a small bulb on the connecting tubing. The adjustment of the mercury—very little of which is required—is simplified by using a screw clip and pinchcock on the tubing connected with the leveling burette.

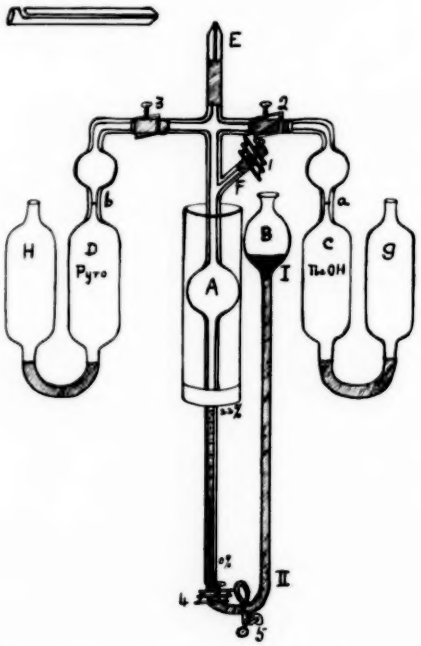
DESCRIPTION OF THE APPARATUS

The gas burette (*A*) is 10 c.c. capacity from the end of the oblique side tube (*F*) to the lowest graduation on the narrow portion. The uppermost graduation corresponds to 2.2 c.c. from the lowest, the distance between the two being divided into c.c. and 1/50th c.c. The bulb part of the stem to just above the 2.2 mark is surrounded by a water jacket. Above the side tube (*F*) the burette is continued into a narrow-bored tube (narrower than represented in the diagram), with two arms at right angles to each other. These are connected by thick-walled pure-gum tubing, with the absorption bulbs (*C* and *D*) containing re-

*It is not suggested that the apparatus herein described should be employed by those accustomed to the use of the standard burettes or where expense is no object.

spectively a 20 per cent solution of NaOH and a 60 per cent solution of KOH with 10 per cent pyrogallic acid dissolved in it.*

Each bulb is connected below by rubber tubing with the overflow bulbs (*G* and *H*). A small bulb (relatively smaller than represented in the diagram) is blown on the stem of each absorption bulb to serve as a trap preventing the solutions from passing over into the burette. The vertical tube above the cross tubes is closed by the *pressure adjuster,* which consists, as shown in the small side sketch in the diagram, of a glass rod beveled at one end and bored most of the way down the center. At a distance of about 3 mm. from where the beveled portion joins the tube a lateral hole is bored to meet the channel in the center. The adjuster is connected by pure-gum tubing with the central tube of the burette, the beveled end of the former being in contact with the end



of the latter. When the rubber tubing is pinched up opposite the side tube, the burette is brought into communication with the outside and the pressure in it remains undisturbed when the tubing is allowed to fall back into place.

The lower end of the burette is connected by thick-walled rubber tubing with the reservoir (*B*), and on this tubing are a pinchcock (*5*) and screw clip (*4*). About 15 c.c. of mercury suffices to fill the apparatus. The reservoir is hung by a loop of wire around the neck on hooks placed on a wooden upright stand, the higher one being in such a position (marked I†) that the mercury stands at the end of the side tube (*F*), and the lower one (marked II) so that it stands exactly at the mark 0% on the burette.

*NaOH may be substituted for KOH, but is not so satisfactory because of its viscosity. The best solution is made by dissolving pure NaOH (electrolytic, if possible) in an equal weight of water, diluting 10 c.c. of this solution with 4 c.c. water, and dissolving 10 gm. pyrogallic acid in the resulting mixture. Shipley: Jour. Am. Chem. Soc., 1916, xxxviii, 1687.

†The position I should be at a higher level than is shown in the figure.

TECHNIC OF THE ANALYSIS

The first step is to fill the tubing between the side tube (F) and the absorption bulbs with nitrogen. This is accomplished by taking a sample of air in the burette by opening screw clip 1, placing the mercury reservoir so that it stands opposite the lower end of the burette (at II), and with the screw clip (*4*) open, cautiously opening the pinchcock (*5*) so that air enters the burette. The screw clip (*2*) is then opened and the reservoir (*B*) raised to position I. By cautiously opening the pinchcock (*5*) the air is made to pass into *C*, and with *5* open the reservoir is raised and lowered several times so that all traces of CO_2 are removed from it by the alkaline solution, after which the reservoir is replaced in position II and the pinchcock, previously closed, opened until the NaOH stands at the mark (*a*) on the stem. Screw clip *2* is then closed, *3* opened, and the oxygen removed from the air by repetition of the same procedure. Screw clip *3* is then closed. This preliminary filling of the burette with nitrogen is unnecessary if a previous analysis has been made.

The sample of gas for analysis is now collected in an all-glass (Luer) syringe with the piston well lubricated with vaseline. With the screw clips (1) open, the burette is filled with mercury up to the end of the side tube (*F*), and the nozzle of the syringe is inserted in the rubber tubing of the side tube. While making this connection the piston of the syringe should be gently pressed so that no air may be allowed to become entrapped in the rubber tubing on *F*. To aspirate the sample into the burette the reservoir is placed in position II and the pinchcock *5* opened, gentle pressure being meanwhile maintained on the piston of the syringe. After the gas has been transferred, the mercury meniscus should stand about 1 mm. below the 0 graduation on the burette, this being accomplished by gentle pressure on the piston of the syringe. This leaves the gas in the burette under a slight positive pressure.

The pressure in the burette must now be made equal with that of the atmosphere. For this purpose the pinchcock (*5*) and all screw clips except 1 are opened, and the tubing on the adjuster (*E*) is pinched opposite the bevel. Being under a slight positive pressure, some of the gas in the burette escapes through the adjuster, and it is during this procedure that a slight error is incurred because some of the sample of gas mixes with the nitrogen above the side tube. The error thus incurred is, however, negligible for most purposes. The meniscus of mercury should now stand exactly at the 0% mark.

Screw clip 3 is now closed. This slightly compresses the gas in the burette and lowers the menisci at *a* and *b*, the new level at *a* being marked on the glass by a glass pencil. The reservoir (*B*) is slowly raised and lowered several times (with 4 and 5 open) so that the gas passes in and out of *C*, in which the CO_2 is absorbed. In doing this, care must be taken that the mercury does not rise above the level of *F*, and that the NaOH solution does not rise higher than the mark *a*. Four movements usually suffice to absorb all of the CO_2.

To determine the volume of the remaining gas, the pinchcock (*5*) is closed, the clip (*4*) half way screwed down, the reservoir placed in position II, and the pinchcock then cautiously opened until the NaOH solution is as nearly

as possible brought back to its original position at *a*. The fine adjustment of this level to the pencil mark is finally effected by means of screw clip *4*. The reading on the burette opposite which the mercury now stands gives in cubic centimeters the amount of CO_2 in 10 c.c. of gas. To make certain that all the CO_2 has been absorbed, the above procedure should be repeated.

To determine the oxygen, screw clip 2 is closed and 3 opened. The level of the meniscus of the pyrogallic acid solution is marked with a glass pencil at *b*. The gas is then moved in and out of D several times, until all the oxygen is absorbed as determined by no further shrinkage. This takes considerably longer than for CO_2. The final volume of gas as read on the burette, less the volume of CO_2, gives the oxygen.

After completion of the analysis the apparatus should be left filled with nitrogen and with the screw clips all closed. A short piece of rubber tubing should also be connected with the upper end of the reservoir (*H*) and closed by pinchcocks. This is to prevent undue oxidation of the pyrogallic solution.

As above remarked, a slight error is incurred in using the above apparatus during the adjustment of the pressures. With a little practice, however, this becomes very small. It is very important to make certain that all the rubber unions are perfectly tight, which is best insured by wiring the tubing.

The following analyses for CO_2 made by Mr. Shen will serve to illustrate the degree of accuracy of the method.

1. Mixture of nitrogen and CO_2 from stock bottle: CO_2, 1.78, 1.79, 1.81, 1.76; average, 1.785. Another mixture: 1.91, 1.99, 1.95, 1.95; average, 1.950.

2. Samples of alveolar air taken in all-glass syringe by using the Haldane tube:

a. Deep expiration after a normal inspiration: 6.03, 5.88, 6.04, 6.09, 5.96; average, 6.00.

b. Deep expiration after a deep inspiration: 5.42, 5.38, 5.33, 5.23, 5.54; average, 5.38.

3. Samples of air aspirated from the mouth after a deep expiration. This was done by placing a short piece of rubber tubing attached to an all-glass syringe at the back of the mouth, closing the lips around it after making a quick forced expiration, and quickly withdrawing the piston, the "dead space" of the tubing having been filled with alveolar air by a preliminary trial of the procedure.

a. Deep expiration after a normal inspiration: 5.76, 6.07, 6.09, 6.10; average, 6.00.

b. Deep expiration after a deep inspiration: 5.42, 5.31, 5.44; average, 5.39.

A CONTRIBUTION TO THE TECHNIC OF ARTIFICIAL RESPIRATION IN MAN*

By G. N. Stewart and J. M. Rogoff, Cleveland, Ohio

THERE is a pretty general agreement that in attempting resuscitation in apparent death by electric shock, drowning, asphyxiation from gases, etc., artificial respiration should be at once begun by a manual method, the best being the prone pressure method recommended by Schäfer. The advantage, in many cases, of supplementing this later on, especially where the artificial respiration must be kept up a long time, by some mechanical arrangement neither liable to get out of order nor likely to be dangerous in the hands of a novice, has been pointed out by a number of writers whose acquaintance with the subject entitles them to speak with authority, and especially by Meltzer. Schäfer,[1] too, has remarked that the method of Horvath (forcing air into a nostril, by a bellows, the mouth being shut) "might well be employed in certain cases," although it "would not be available in most instances of apparent death from drowning; but its efficiency should not be forgotten, especially since it appears to afford a means of forcing air into the alveoli in cases in which the more gentle current of air which is produced by movements of the ribs, fails to find a passage through the frothy mucus which may partially block the bronchi."

Meltzer[2] quoting largely from Keith[3] points out that inflation of the lungs by bellows was long the accepted method in resuscitation of the apparently drowned. It seems to have been discontinued on quite insufficient grounds. Anyone who has had experience of the routine methods of artificial respiration in animals in the laboratory, which can easily be carried on without any cutting operation by the use of a properly shaped mask or by laryngeal intubation,[4] is aware of their great superiority over manual methods for long-continued respiration.

Meltzer has described a simple arrangement[2] which he considers superior to any of the more elaborate and expensive devices put upon the market by commercial firms. The current of air, maintained by a foot bellows, is interrupted at the desired rate by a respiratory valve actuated by a lateral movement of the thumb. A rubber bag is interposed between the bellows and the valve. Meltzer discards the close-fitting mask on the ground that the danger of infected material being forced into the lungs is increased by its use. For the mask he substitutes a pharyngeal tube of appropriate shape and size, the air being thus delivered to the patient by "pharyngeal insufflation." Others have raised objections to the "close-fitting" mask, and some have included in their condemnation all mechanical devices, the use of which according to them occasions neglect of the manual methods and delay in starting artificial respiration while the apparatus is being procured.

We have examined two forms of apparatus, Meltzer's and the commercial

*From the H. K. Cushing Laboratory of Experimental Medicine, Western Reserve University.

apparatus known as the "lung motor." Meltzer has shown that efficient respiration is easily maintained with his arrangement; a curarized dog, for example, being kept alive indefinitely. Although it seemed sufficiently obvious that this must also be the case with a pump like the "lung motor," we thought it worth while to demonstrate the point. There is no difficulty in maintaining with it efficient respiration indefinitely in a curarized dog. Of course, the mask must be of appropriate shape to fit a dog. One of the metal cones used for giving ether was found to answer admirably. A piece of sheet rubber was tied over the wide end and a round hole cut in the rubber, through which the dog's snout was pushed. The narrow end was closed by a cork, a tube in which communicated with the respiration apparatus. The animal's tongue was drawn out under the rubber and secured. This device is a convenient one for giving artificial respiration to animals which are to be allowed to survive, in an experiment or operation in which it is needed. It is theoretically an objection to the "lung motor" that the expiration is accomplished by a suction action of the pump. With a small animal the sounds accompanying this suction, extending widely over the thorax and even the abdomen, although apparently generated at the larynx, are alarming, but it was not possible to demonstrate that any harm was being done, so far as could be seen from the blood pressure curve or at autopsy. With a large animal the suction sounds were much less obtrusive. At the same time Meltzer's objection that this suction in expiration is unnatural and unnecessary seems to us a valid one, and it certainly seems better to allow the expiration to take place by the elastic recoil when the inflation ceases.

The foot bellows, with a rubber bag interposed, as recommended by Meltzer, appears to be the simplest and most practical method of obtaining the necessary pressure for inspiration. However, while there is no doubt that in skilled hands the pharyngeal tube is safe and efficient, we prefer a mask, as being simpler to adjust and better for general use. We believe that the mask for ordinary use should not be fastened in any way but merely held by the operator on the patient's face. This permits its removal at any moment for cleansing or for clearing out the mouth, and its immediate readjustment. We have also substituted for Meltzer's respiratory valve the valve shown in Figs. 1 to 3 (two-thirds of the actual size). The valve, constructed of aluminum, consists of a tube *T* (Fig. 1), one end of which is attached to the mask and the other end to a rubber bag kept filled with air by a bellows. A plunger *P*, is pressed in by the thumb or by the palm of the hand at the rate of fifteen to twenty times a minute. It is convenient to hold the valve with the four fingers applied to the tube, the plunger passing between the middle and ring fingers. When it is pressed in air passes through a hole bored across the plunger, and traversing the tube inflates the lungs. The position of the plunger in inspiration is shown in Fig. 2. The spring *S* (Fig. 1) is compressed as it goes in, and returns the plunger by its recoil as soon as the pressure ceases, allowing air to escape from the lungs through a hole bored longitudinally from the lower end of the plunger and then radially so as to open at one side of it, as shown in Fig. 3. The plunger carries a pin (*p*) which engages in the slot (*s*) and can move freely down the slot when the plunger is pushed in but can not return beyond the top of the slot when it is released. This prevents the possibility

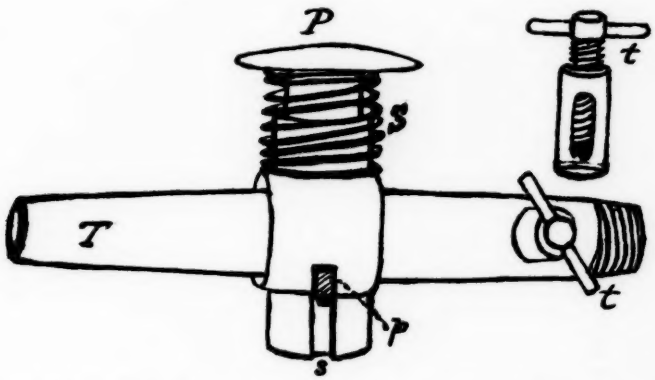


Fig. 1.—Respiration valve. *T*, tube through which air passes; *P*, plunger; *S*, spring; *p*, pin on plunger; *s*, slot in which *p* works; *t*, thumb-screw of safety opening shown separately in right-hand corner of figure.

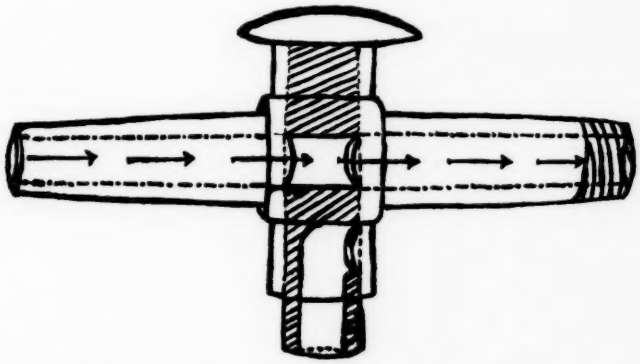


Fig. 2.—Section through respiratory valve showing position of plunger in inspiration.

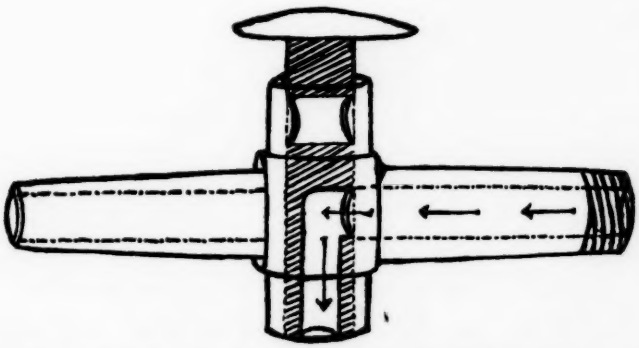


Fig. 3.—Section through respiratory valve showing position of plunger in expiration.

of the plunger coming out during the artificial respiration. A small thumb screw (*t*, Fig. 1) in a short side tube near the mask end of the tube *T* constitutes a safety arrangement to prevent the possibility of excessive pressure inside the mask. The side tube is slotted for the chief part of its length and by moving the screw, a greater or smaller permanent opening can be produced. The screw is arranged so that it is impossible to close the slot completely. The making of the safety arrangement and the valve in one piece we consider an improvement of some value, as it reduces the number of parts of the apparatus and, therefore, the time spent in connecting it up. A similar advantage is gained by the attachment of the valve directly to the mask. This also diminishes the dead space of the apparatus.

The valve can be taken apart in a moment for cleansing. To do this the plunger is removed by unscrewing the top. It is then easily pushed out of the tube *T*. The safety thumb screw (*t*) is also removable. The valve can be worked with great ease for long periods without fatigue. It can be operated by pressing with the first phalanx or the ball of the thumb or the palm of the hand. The valve is intended to be fastened to the mask so that one of the operator's hands suffices to work the valve and to hold the mask against the face, leaving the other free.

Since the operator may have to carry on the artificial respiration with the patient on the ground, an attachment has been fitted to the bellows which allows it to be worked conveniently by one forearm or one hand as well as by the foot. A wedge-shaped piece of wood is fastened to the top of the bellows so that its upper surface is nearly horizontal before compression. On this is hinged strongly a piece of wood about as long as the forearm. The hinge is situated at the edge of the bellows but the support projects two or three inches so as to increase the leverage. When the forearm is to be used, as is convenient when the operator is sitting down, the hinged piece is folded back over the bellows. The elbow is placed at the hinged end and the fingers project beyond and grasp the free end. Little effort is necessary in this way to keep the bellows going. When the hand is used, and it of course postpones fatigue in a long artificial respiration to vary the mode of compressing the bellows, the hinged piece is folded out so that it projects from the bellows and constitutes a lever.

As regards the question of what should be taught to the layman, our experience is in favor of teaching the immediate application of a manual method, followed by, or alternated with the employment of a simple mechanical device, when such is available. We do not believe that the average workman if taught to immediately begin with a manual method, the reason for this being sufficiently emphasized, and practiced in applying the mechanical device only later on when all is ready, will be at all likely to sit down and do nothing until an apparatus is procured.

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AN ADJUSTABLE TRACHEA CANNULA*

By John A. Higgins, Chicago, Ill.

If a laboratory worker, on animal experiments, were to visit other laboratories outside of the line in which he is directly concerned, the indications are that he would see various types of trachea cannulas in use by the various laboratory workers. Some laboratory workers prefer an ordinary piece of glass tubing for a trachea cannula. This piece of glass tubing is generally connected to a long piece of rubber tubing, which in turn is connected either directly or indirectly to an ether container. Where this method is used, the laboratory workers seem to consider as minor factors such points as the increased accumulation of carbon dioxide, which the lungs are constantly giving off with each exhaled breath, the increased amount of labor concerned in breathing through a long space of tubing, together with a constant loss of ether where air is inhaled and exhaled through the same ether container.

Another type of trachea cannula is the T-tube type. This type of cannula is best illustrated by Jackson.† Other types of trachea cannulas on the market are the ones manufactured by the Harvard Apparatus Company, Boston, Mass.; Charles Verdin, Paris, France; E. Zimmermann, Leipzig; etc.

A cannula which I have devised and which I wish here to describe can be used in the laboratory with attachments and for other uses. I have kept in mind the object of making a compact yet useful piece of apparatus and eliminating unnecessary dead space.

The cannula (Fig. 1) is made by taking a piece of ½ inch brass tubing 3½ inches long and making into an L-shaped piece by cutting or filing to the lower inside edge a V-shaped cut and using the uncut section of the V as a basis to make the L-bend upon.

On the front end of the L is soldered a short piece of 5/16 inch brass tubing (*A*). On the lower section of the L is soldered an outlet of ½ inch brass tubing ¾ inch long (*B*). On the upper surface of both the lower ½ inch pieces just described, and ¼ inch from the end of the tubes, are soldered small tits of a No. 12 or 14 gauge brass wire ⅛ inch high (*C*).

On the upper section of the L-piece is arranged a piece of telescope tubing, 9/16 inch by 1/32 inch wall brass tubing, and on the same order as the air regulator of a Bunsen burner with the exception that while a Bunsen burner has two air-hole regulators, the piece of tubing at this point is provided with one air-hole exhaust vent (*D*).

Just above the air regulator, or exhaust vent, is a valve chamber. This chamber is cup shaped, made from a piece of 11/16 inch tubing ½ inch high. It contains a ½ inch hole in the bottom and four smaller exhaust holes on the side. To the upper outside edge is fastened a ⅛ inch lip of sheet metal to

*From the Department of Physiology, University of Illinois School of Medicine.

†Jackson, D. E.: Experimental Pharmacology, 1917, St. Louis, C. V. Mosby Co., p. 87, Fig. 7.

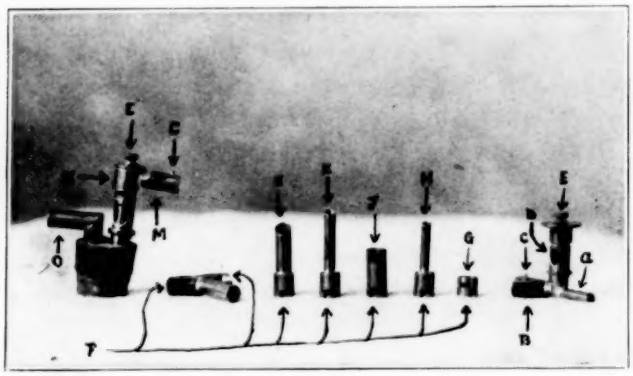

Fig. 1.—Showing individual parts of an adjustable trachea cannula. For description see text.

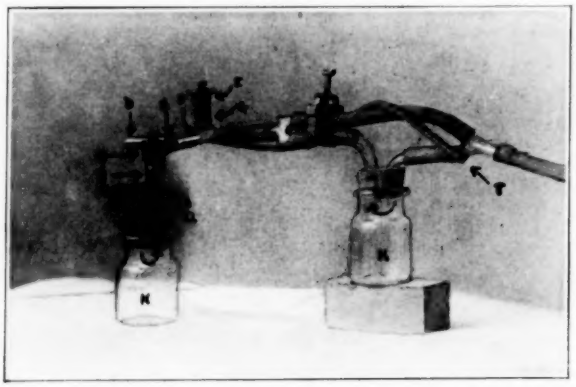

Fig. 2.—Adjustable cannula arranged for ordinary experiments and connected to artificial respiration tube. *K*, ether container and *T*, tube to tambour. For description see text.

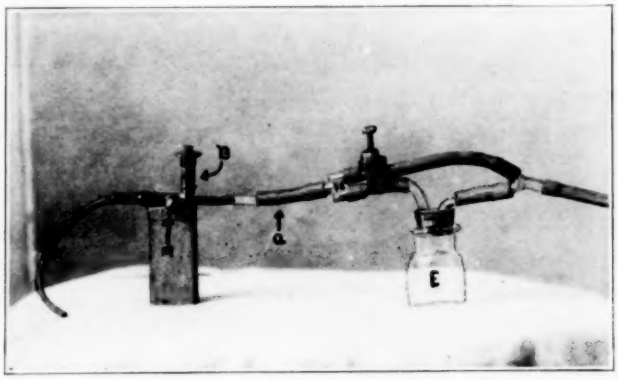

Fig. 3.—Adjustable cannula arranged for intratracheal insuffation experiments. *E*, ether container. For description see text.

which is fastened the lid by means of two screws coming through the lip and lid from the bottom, a No. 2/56 size screw being used.

Running down through the upper lid is a No. 8/32 set screw (*E*) which is used to lock the valve in the valve chamber when the valve is not in use. This set screw is of such a length and type that it snugly closes the valve and then automatically locks itself by a shoulder hitting the upper side of the lid. This also prevents further penetration or injury to the valve. The valve is a small disk of thin sheet copper about a 32-gauge coil spring wire. The coils of this spring wire should be about ⅛ of an inch apart. The object of the coil spring is simply to keep the disk in an upright position and prevent its sticking to the lid, a result which might be caused by the exhaled vapors.

To the lower ½ inch L-piece can be fastened various sized reduction tubes to accommodate different sized animal tracheas. These reduction tubes are made up by fastening any desired sized tubing, up to ½ inch, into a piece of solid brass rod ⅛ inch long by ½ inch round. A piece of brass tubing 9/16 by 1/32 inch and ¾ inch long is then taken, and on one end is cut out a ⅛ inch wide L-piece (*F*). This L-piece is simply cut out and used in the fashion of a lock with the small tit pieces previously described and shown at (*C*). The reduction tube is fitted snugly into a hole in the ⅛ inch long by ½ inch rod. The 9/16 inch by ¾ inch tube is made to telescope the ½ inch piece, with the cut end exposed, and the three pieces of metal are now soldered solid.

To the side outlet of the L, and in a similar manner as previously described, can be attached either a sealed piece of tubing (*G*); a straight tube connection (*J*); a T-tube connection (*I*); or a reduction tube (*K*). For ordinary blood pressure work, I would suggest using either a straight tube or a T-tube connection. Where artificial respiration may have to be resorted to, I would suggest the latter connection for use in the experiment.

At *M* (Fig. 1) is another piece of ½ inch tubing which connects with the straight tube or T-tube. This short piece of tubing is soldered to the side of valve chamber (*N*), which chamber, although of a slightly different outside appearance from the valve chamber previously described, is in reality built on the same general principles—a disk, coil spring, and set screw to lock the valve.

To the lower end of this valve chamber is soldered a piece of ½ inch tubing about 3 inches long. On the upper end of this tube is an air regulator similar to the one already described. The remainder of the ½ inch tube is used to fasten into a cock stopper, which stopper in turn is fastened into the neck of a bottle or other ether container. At *O* (Fig. 1) is another small ½ inch L-tube which penetrates through another section of the same cock stopper. This L-tube, however, can and should be omitted and was added solely to indicate an air passage to the ether container.

Where the T-tube is used as the connecting link between the cannula proper and the ether container section, the open end of the T-tube can be connected by tubing to the source of artificial respiration. I have devised a new type of adjustable screw clamp in connection with this cannula which I shall report in another article. The advantage gained, with the T-tube at this point, is to keep the artificial respiration tubes constantly connected, without

any fear of interfering with normal breathing, and to eliminate loss of time or trouble involved in making tube connections, etc., which trouble I have witnessed in animals at the last minute when respiratory movements were the main issue of revival.

The short piece of 5/16 inch tubing, on the front end of the cannula, can be used with a tambour to record respiratory changes in the air system after the apparatus is connected and regulated for an experiment. This method of recording respiration will eliminate other simple methods; i. e., the stethograph drum method, the thistle tube, membrane and cock method, etc. Where the two last-mentioned methods of recording respiration are concerned, it must be considered that respiratory movements have a tendency to shift from the thoracic to the abdominal region or vice versa.

For ordinary experiments the apparatus ready for use will appear as illustrated in Fig. 2. On inspiration the air and ether vapors pass respectively through tube *A*, past the valve in valve chamber *B*, through tubes *C* and *D* and into the lungs, the valve in valve chamber *E* locking itself on inspiration. On expiration the valve in valve chamber *B* locks itself and forces the expired air through tubes *D* and *F* past the valve in valve chamber *E* and to the outside air. If the ether vapors, on inspiration, are too condensed, the anesthetist will be able to reduce such density by regulating the air inlet at *H*.

Where artificial respiration is desired, open air outlet at *G* (Fig. 2), lock valve in valve chamber E with the set screw and then gradually close the air outlet *G* until the desired flow of air is present. In cases where the artificial respiration is accidentally turned on into the system, previous to opening air outlet *G*, the valve in valve chamber *E*, if not locked, will act as a safety valve for any excess pressure in the lungs.

Where an intratracheal insufflation experiment is to be carried out, this apparatus can be so adjusted as illustrated in Fig. 3. This arrangement may be had by using the trachea insertion section as usual, connected with the cannula proper section, to the side outlet of which has been added reduction tube *H* (Fig. 1). To operate, insert cannula into the trachea in the usual manner. Next insert a thin-walled rubber catheter or a piece of 1/4 inch black gum rubber tubing that will fit snugly into the 5/16 inch tubing on the front end of the cannula. One end of this tubing should extend about 6 or 7 inches down the trachea of an average sized animal (dog). The other end of the tube should be connected to a reducing tube that will connect onto the air and ether vapor tube outlet. To reduction tube *H* (Fig. 3) is connected, by means of a rubber tube, a manometer to gauge the pressure used to inflate the lungs. With the air and ether vapors entering the lungs through tube *A* and with the valve in the valve chamber locked, it will then be only a matter of judgment to regulate outlet *B* and gauge the pressure desired to proceed with the remainder of the experiment.

A NEW TYPE OF ADJUSTABLE SCREW CLAMP*

By John A. Higgins, Chicago, Ill.

IN a previous article[1] I referred to a new type of adjustable screw clamp. This type of adjustable screw clamp was devised with the object of giving the anesthetist, and in certain animal experiments, a more perfect control of the air and ether vapors employed. Where the thoracic cavity has been exposed for work on the heart, lungs or other thoracic cavity structures or where intratracheal insufflation experiments are being carried out on the mammalian animal, it seems a customary procedure to control such animals with artificial respiration and ether.

The type of adjustable screw clamp heretofore employed in controlling air and ether vapor during an experiment, as previously mentioned, is best illustrated by Jackson.[2] With this older type of screw clamp the following few points are involved; that each tube requires an individual screw clamp; that it involves two separate operations to clamp down on one tube, while you release the pressure on the second tube; that there is more or less danger of unintentionally clamping down on one of the tubes before releasing the pressure from the second tube, etc.

Such points, as just mentioned, have been eliminated in this new type of screw clamp. The new type of screw clamp can be utilized on single tubes, and in the same way as the older type, with the added advantages. Each screw clamp can control two tubes in a single air and ether vapor system. The clamp is foolproof, and one can not close one tube without, at the same time, automatically releasing the pressure from a second tube, thus eliminating any danger of resistance in the artificial respiration system. Also the two, air and ether vapor, tubes involved can be regulated in one operation of adjustment.

This new type of screw clamp which I shall describe, and which is illustrated in Fig. 1, was made up from scrap pieces of copper rod taken from worn-out zinc battery plates. Since one can dispense with soldering joints in this new type of clamp I might suggest the use of a cheaper metal if available in the construction of other clamps of this type. The dimensions, as will be described, in connection with this screw clamp, were figured out to accommodate the use of one-half inch red antimony or white gum heavy walled tubing which in my opinion seems to be the most suitable variety of tubing for artificial work.

The clamp is made by taking a piece of $\frac{1}{8} \times \frac{3}{8}$ inch rod and bending in the vise a four-sided piece, making the bends on the larger flat surface, whose inside dimensions measure $\frac{7}{8}$ inch by one inch. The ends can then be fastened solid with No. 2/56 or smaller size screws. Care must here be taken to thread both ends and file the excess end of the screw away.

A U-piece is made up with the same size material, which piece should fit with slight play around the two long sides and one short of the four-sided piece previously described. The next step is to file down about $\frac{1}{32}$ of an inch from the $\frac{1}{8}$ inch surface of the four-sided piece or enough to allow a little play between the inside surfaces of two horizontal bars extended across the open, narrow and side ends of the U-piece. Now drill a No. 30 gauge hole in the

*From the Department of Physiology, University of Illinois School of Medicine.

[1]Higgins, John A.: This Journal, page 77.

[2]Jackson, D. E.: Experimental Pharmacology, St. Louis, 1917, C. V. Mosby Co., p. 111.

middle of one of the short, flat surfaces of the four-sided piece and thread this hole with a No. 8/32 tap.

Two pieces of the rod about ¾ inches long are then taken. In the middle of one and on the flat surface is drilled a hole that will permit a No. 8/32 screw to slip through easily. The hole is then countersunk and in such a fashion as to permit a small burr on the end of a No. 8/32 screw to slip around easily, but not so as to pull away. The countersunk surface of this piece is set against the flat surface of the yet undrilled short piece. Both pieces should be held firmly together and a No. 49 gauge hole drilled through both pieces, going through the flat surfaces close to the ends, and finally threaded with a No. 2/56 tap.

A No. 8/32 screw of about 1⅜ inches long, having a suitable head to work with the fingers, is taken and screwed from the outside into the 8/32 gauge

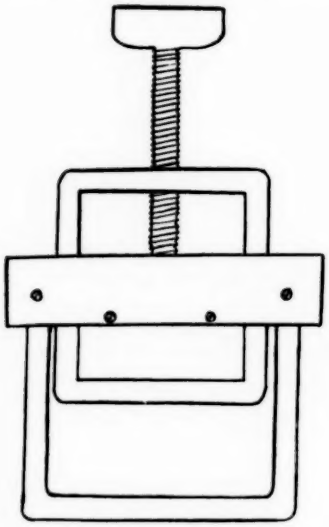

Fig. 1.—Pen and ink drawing of new type of adjustable screw clamp.

Fig. 2.—Showing new type of adjustable screw clamp in position on air and ether vapor (artificial respiration) tubes. For description see text.

threaded hole as previously made on the four-sided piece. Now place the short countersunk piece on the threaded end of the 8/32 screw, with the countersunk surface facing the opposite side of the 8/32 threaded section. A burr is then riveted to the threaded end of the 8/32 screw and the other short flat piece is fastened with 2/56 screws to the countersunk surface of the former mentioned countersunk piece. File away the protruding ends of the 2/56 size screws at this point.

Two horizontal bars, or a strap-like piece that will extend around the ends of the U-piece are now fastened evenly to the loosely fitted block and at the end of the 8/32 screw and fastened with 2/56 size screws. The U-piece is lastly slipped between the horizontal bars and fastened with screws of a 2/56 size. It is now a matter of judgment on leaving the screw heads, just set in, intact or filed away to come flat with the other metal surfaces. I have in my case taken the latter view. Fig. 2 will indicate the appearance as set on two tubes ready for service.

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EDITORIALS

The Bacteriology of Influenza

IN 1892 Doctor R. Pfeiffer announced his discovery of a bacillus which he believed to be the causative agent in epidemic influenza, and this claim seems to have met with ready and general acceptance. Pfeiffer examined sputum brought up from the bronchi. This was spread upon sterile glass plates, and the loop was taken from the purely purulent portion. The best preparations were made by staining with a dilute carbol fuchsin. It was found that the stain penetrates slowly, and the cover-glasses were allowed to float for from five to ten minutes in the solution. Pfeiffer made the following statement:

"In preparations of influenza sputum made under the above described precautions, we found in all recent and complicated cases a single, well-characterized species of bacillus in almost absolutely pure cultures, and always in surprising numbers. The bacilli are situated mostly in the form of nests and swarms in the mucous ground substance of the sputum. They are found also in greater or smaller number in the protoplasm of the pus cells where they are grouped around the nucleus without ever penetrating into the nuclear substance.

The influenza bacilli have not quite the transverse diameter of the bacilli of mouse septicemia. Their length, as a rule, is only two or three times their width, though occasionally we discover in the sputum, and sometimes in pure cultures, longer organisms that are to be regarded as filaments. In older pure cultures of from three to four days' duration, very long filaments may occur, but these are abnormal forms, the first signs of beginning involution. The ends of the influenza bacilli are rounded. Very often we found two particularly short bacilli in close apposition. These are forms of division that are apt to be interpreted as diplococci, and undoubtedly have been mistaken for them. The bacilli have no capsules and are nonmotile. They are gram negative, and in faintly stained specimens it is sometimes noticed that the poles are more deeply colored than the middle portion."

Pfeiffer was not able to grow these organisms upon gelatin or agar plates either aerobically or anaerobically, but he did grow them upon media containing blood, and ascertained that hemoglobin is the blood constituent essential to their growth.

Oxyhemoglobin is not essential, and boiling does not lessen the efficiency of the hemoglobin in the culture medium. On blood agar the colonies are minute droplets and when crowded can be seen only with the aid of a lens, but in sparse growths they may be seen by the unaided eye. The colonies have a glassy transparency and under the microscope appear to be without structure. The bacilli are strictly aerobic, and grow quite abundantly in bouillon containing hemoglobin. They do not multiply below 30° or above 43°. In drinking water they soon die, and they are very sensitive to drying.

From his experiments Pfeiffer came to the conclusion:

1. Any development outside the normal body, in the ground or in water is impossible.

2. The spread of the disease through dry sputum can occur only to a limited extent.

3. The contagion, as a rule, is conveyed by the recent, still moist culture from the nasal and bronchial mucous membrane of influenza patients.

4. Kitasato showed that pure cultures may be obtained directly from the sputum. The patient coughs the bronchial sputum into a double sterile dish. The sputum is thoroughly dissected with sterile needles, and during this process of disintegration it is carried through ten successive washings with sterile water. A bit of the washed sputum is examined microscopically and another portion is inoculated on the blood agar.

In uncomplicated influenza Pfeiffer found the bacilli in all cases in pure cultures in the bronchial sputum. When the influenza was engrafted on an existing bronchial affection, or when the influenza was complicated with bronchitis or pneumonia, other organisms were, of course, found in the bronchial sputum. Pfeiffer did not find the organism in the blood. The bacilli may persist in the sputum for months after recovery, and thus the individual may become a chronic carrier and distributor.

Pfeiffer's attempts to transmit the disease to mice, rats, rabbits, guinea pigs, swine, dogs and cats were wholly without result. His experiments with monkeys are worthy of recall at this time. Into the trachea of one of these ani-

mals he injected a flake of sputum the size of a pinhead, which had been found to be a pure culture, mixed in 1 c.c. of bouillon. The animal died after indefinite symptoms, and postmortem showed an abscess the size of a walnut at the site of inoculation. The pus of this abscess showed a few intact influenza bacilli and no other bacteria. Three monkeys had similar injections into the lungs through the thoracic walls. Some elevation of temperature took place after from twenty to thirty hours. The fever was remittent and transient. The animals coughed, but showed no typical influenza. Two weeks later they were reinoculated and developed milder symptoms. One was inoculated in the nose and showed a slight fever. Still another received an injection in the trachea and developed a temperature of 39.2° the same day. The next day the temperature began to fall and death resulted within forty-eight hours after inoculation, the temperature reaching 32.2°. This was not an infection, but an intoxication.

Rabbits died after a few hours from intravenous injection of the bacilli, but this results from similar treatment with the cellular substance of bacteria, known not to be pathogenic. Kruse made further animal experiments with the same lack of success. Up to the present time all attempts to induce influenza or any other infection in the lower animals with this organism have failed. The cellular substance contains a poison, but so do all proteins. We are compelled to conclude that it has not been proved that the Pfeiffer bacillus is or carries the virus of the disease we know as influenza. It may be a frequent, possibly a constant, accompaniment of the disease, but this does not prove that it is the cause.

—*V. C. V.*

Influenza Epidemic

THE following letter was sent out under date of October 16, 1918, by the Volunteer Medical Service Corps, Council of National Defense, to members of state executive committees and county representatives of the Volunteer Medical Service Corps:

"1. In view of the present serious epidemic which is sweeping over the country, the Volunteer Medical Service Corps earnestly invites your attention to the following important action:

"Urge upon the members of the Volunteer Medical Service Corps that they instruct families under their care to guard against the epidemic by:

"Thorough cleanliness of houses, premises, clothing, utensils, and personal cleanliness.

"Avoid stirring up dust.

"Wash; scrub; flush; sprinkle; and use soap and water thoroughly.

"Gargle and spray the nose and throat with an alkaline antiseptic fluid frequently.

"Cooperate at once to the fullest extent with the Local, State, and National Boards of Health. Urge and cooperate in preparing towns and cities for the epidemic by establishing emergency hospitals in suitable buildings, by district-

ing communities, and apportioning or dividing medical forces comprising men and women physicians and nurses so that no portion of the community is without medical care.

"Circulate as thoroughly as possible and explain to the public the warning and directions printed by the United States Public Health Service and by local health authorities.

"Urge the importance of fresh air and the avoidance of chill and overheat.

"In fighting the epidemic give no medicine and use no treatment which may depress the vital forces, especially the heart of the patient.

"2. The Army and Navy are fighting and conquering Germans. We must fight and conquer germs without taking anything away from the Army and Navy. Don't ask the Army and Navy for medical and surgical supplies. Use simple utensils for sterilizing; the simplest kinds of beds and bedding; make your own masks and dressings, and fight for yourselves.

"3. While the epidemic is on, do no surgical operations unless absolutely necessary to save life.

"4. In every way in your power urge the members of the Volunteer Medical Service Corps to cooperate to the fullest extent with the United States Public Health Service and with State and Local Health Authorities.

(Signed) EDWARD P. DAVIS,
President, Volunteer Medical Service Corps.

ERRATUM

In the article entitled "The Treatment of Dichlorethylsulphide ('Mustard Gas') Injuries," by Aldred S. Warthin, Ph.D., M.D.; C. V. Weller, M.S., M.D.; Capt. Lester Roos, M.D., and G. R. Herrmann, M.S., M.D., in the October, 1918, issue of the JOURNAL, page 848, the thirteenth line should read "use of .5 per cent solution" instead of "5 per cent solution."